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THE INFLUENCE OF ALCOHOL AND OTHER DRUGS ON FATIGUE

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THE CROONIAN LECTURES DELIVERED AT THE ROYAL COLLEGE OF PHYSICIANS IN 1906

BY

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PREFACE

The lectures printed in this book differ from those delivered at the Royal College of Physicians in some details of arrangement, and in the addition of new matter derived from later work ; but the changes have not altered the general character of the lectures, nor have the additions rendered necessary any essential modification of views expressed when they were delivered.

I am glad here to express my thanks to the Royal College of Physicians for appointing me to be Croonian Lecturer, and for allowing the funds of the Croonian Trust to be devoted to the expenses of the researches on which the lectures are based. Many of these researches have been carried out in conjunction with Mr. H. N. Webber, to whose help I owe very much. Others were made in conjunction with Mr. W. McDougall, and I am greatly indebted to him for allowing me to take part in the early trials of his new and most valuable method of studying mental fatigue.

I have also to thank Dr. W. E. Dixon for his help in preparing the mixtures in which the drugs of my experiments were taken, and Professor Langley for allowing me to reproduce some of the illustrations from the *Journal of Physiology*.

W. H. R. RIVERS.

St. John's College,
Cambridge,
December, 1907.

CONTENTS

LECTURE IV (*continued*)

ACTION OF COCAINE, STRYCHNINE, TOBACCO, ETC.

THE

INFLUENCE OF ALCOHOL AND OTHER DRUGS ON FATIGUE

LECTURE I

INTRODUCTION AND METHODS

Introduction—Methods of studying muscular fatigue; fatigue of isolated muscle and general fatigue—Mental fatigue; the curve of work and the curve of fatigue—McDougall's method of studying fatigue of attention—Immediate and prolonged effects of drugs—Methods for investigation of effects of drugs; elimination of influence of interest, sensory stimulation, and suggestion by means of disguise.

In my choice of a subject for these lectures, I have been guided by the desire to show that the science which I teach may be of service to medicine. In accordance with this idea, I shall limit myself to those aspects of the subject which seem to fall within the province of the experimental psychologist. Thus, I shall only deal explicitly with the methods and results of the experimental observation of the living man, though in any theoretical consideration of these results I may have to draw attention to the phenomena of fatigue, as studied on the lower animals by purely physiological methods.

In every experiment on man there come into play certain psychological factors which are wholly absent in the work of the physiological pharmacologist, and it will be my object in these lectures to consider these factors especially, and to develop the methods by means of which they may be studied; in other words, it will be my chief object to consider the

application of pharmacological methods to the study of the living man.

It is necessary at the outset briefly to consider the definition of fatigue. Attempts have been made to define this condition by means of its physiological causes, and even to distinguish two conditions—fatigue and exhaustion—the former depending on the accumulation of the poisonous products of activity, and the latter on the exhaustion or diminished supply of the substances necessary for the continuance of activity ; but, however satisfactory these definitions may be ideally, their application is wholly impracticable in the present state of our knowledge, even in the case of the fatigue of isolated muscle, and still more so in the case of general bodily fatigue or of mental fatigue.

We must be content with some less ambitious definition ; and, taking fatigue as a general term applicable to both bodily and mental states, it may be defined as a condition of lowered capacity for work, which follows or occurs during the performance of work of which it is the direct result.

Further, a distinction must be made between the sense of fatigue—the sensations which supervene during the performance of work—and the lowered capacity for work, shown objectively by diminution in the amount of work executed. These conditions, which may be spoken of as subjective and objective fatigue respectively, do not always run parallel courses. In the performance of mental work especially, decided sensations of fatigue may be experienced when the objective record shows that increasing and not decreasing amounts of work are being done ; and there may be complete absence of any sensations of fatigue when the objective record shows that the work is falling off in quantity, or in quality, or in both.

This distinction is one of great importance for our present purpose, for one of the problems which will have to be considered is whether the apparently beneficial effects of a drug on fatigue may not sometimes be due, not to any direct action on the capacity for work, but to its influence on the

sense of fatigue, diminishing those unpleasant sensations which act as our natural warnings that we are approaching the limits of most favourable activity of our organs. It is obvious that a drug which acts in this way would not be exerting a real beneficial action in fatigue, but would be rather acting as an accelerator of exhaustion, and the problem whether certain drugs act in this way will be one of the questions to be considered in these lectures.

Muscular Fatigue.

In nearly all the work which has been done on the action of drugs in muscular fatigue Mosso's ergograph has been used, either in its original form or with various modifications. Objections have been made that this method does not give a true picture of the normal course of fatigue, and, so far as the single ergogram is concerned, there can be no doubt that this is true. It is now known that the typical Mosso's ergogram is the resultant of a very special set of conditions working together. It has been shown by Treves[1] that the condition of complete exhaustion which occurs at the end of the ergogram is only apparent, and that the weight has only to be somewhat diminished for the finger to become again capable of contractions equal in extent to those of the wholly unfatigued condition. The ergogram of Mosso only occurs with a constant weight near the limit of the powers of the subject of the experiment.

Treves[2] has devised a method of ergography in which the weight can be easily varied, and he has called this the method with variable weight, as opposed to the method with constant weight of Mosso. He suggests that the true course of muscular fatigue would be represented by a curve showing the amounts of the successive diminutions of the weight—a curve which falls most rapidly at first and then more slowly,

[1] *Arch. ital. de Biol.*, 1898, t. xxix., p. 157, and t. xxx., p. 1. Also *Arch. f. d. ges. Physiol.*, 1902, Bd. lxxxviii., S. 7.

[2] *Arch. ital. de Biol.*, 1901, t. xxxvi., p. 44.

till it passes into a horizontal line corresponding to the weight with which work can be continued for an indefinite time.

The interest of this curve arises from the fact that it corresponds closely with the fatigue curve, which is obtained by another method—the spring or dynamographic method. In this method fatigue is produced, not by lifting a weight, but by contracting a muscle or group of muscles against the force of a spring. This method has in recent years had many advocates, as one theoretically more satisfactory than the weight method. The kind of curve produced is of the same nature as that suggested by Treves as the result of the ergographic method with variable weight. The correspondence of these two methods raises the question whether the ergogram of Mosso is not an artificial product, which stands in no definite relation to the true course of muscular fatigue.

The objections to Mosso's method of measuring fatigue are very greatly diminished if, instead of taking a single ergogram as a measure of fatigue, series of such ergograms are recorded at intervals insufficient to allow complete recovery from the fatigue induced by the ergogram. If the amount of work done in such a series of ergograms is represented in the form of a curve, there is usually found to be a rapid fall at first, gradually becoming less, till after a time the successive ergograms show little variation from one another and reach a constant level, the curve representing the course of a series of ergograms thus showing a close correspondence with those obtained by the dynamographic method and by the method of Treves. In my own work I have been chiefly interested in the influence of certain psychical factors which I believe to have had a great effect on the results of previous workers, and as nearly all these workers had used Mosso's method, I had no hesitation in using it in my own work to test the influence of the factors in question; and my experience of the method has shown me that, whatever may be the objections to the single ergogram, the ergographic method with constant weight gives a very valuable picture of the course of fatigue

when series of ergograms are recorded, and is a most useful method for the study of the action of drugs.

If, instead of giving the muscle its maximum task with Mosso's ergograph, a weight sufficiently small is chosen, it is well known that the muscle is able to continue its contractions for an indefinite time; if, then, the weight is slightly increased, it will be found that exhaustion will only show itself at the end of, say, an hour; with a still heavier weight at the end of half an hour, the curves produced being sometimes known as 'Maggiora's curves.' A method which has been used to test the influence of a drug is to determine the time required to induce fatigue with and without the drug. Fatigue which comes on at the end of half an hour in the normal condition may only supervene at the end of an hour, or *vice versa*, and this method, which has been very little used, may be a valuable accessory means of studying muscular fatigue.

My own ergograph is the latest form of Kraepelin's modification of Mosso's ergograph, in which the chief improvements are that the movement is rigorously limited to one joint, and that the fingers are inserted in graduated fixtures by means of which the hand can always be placed in the same position.[1] One can thus be certain that the point of application of the weight and its angle of application are constant. A further improvement is that there is an arrangement by which the weight does not fall back during the relaxation of the finger, and this is combined with another feature which effects a great saving of time, in that the height through which the weight has been lifted can be read directly, and has not to be calculated by measuring the heights of the individual contractions.

In my own work I have adopted the procedure of recording sets of ergograms, the interval between the successive ergograms of a set being always two minutes, and the interval

[1] For a description of the chief features of this instrument see Kraepelin's 'Psychologische Arbeiten,' 1896, Bd. i., S. 380, and 1904, Bd. iv., S. 189.

between any two of the contractions by which the ergogram is formed two seconds, the finger being contracted with one and relaxed with the next beat of a metronome beating seconds. Usually each set has consisted of six ergograms, and the interval between successive sets has been either half an hour or an hour. The weight has been hidden from the view of the subject, and the kymograph on which the

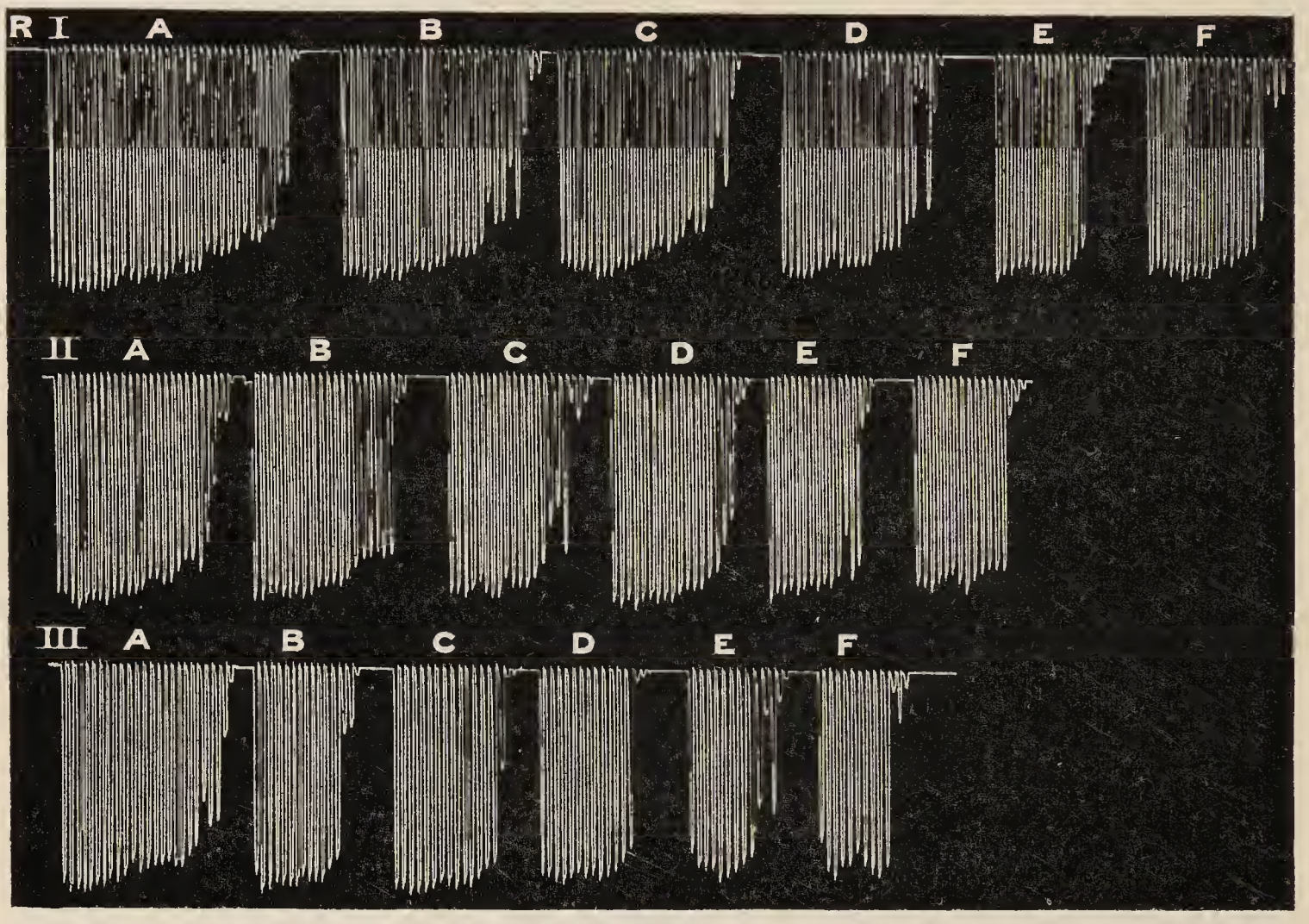

Fig. 1.

ergograms are recorded has been so arranged that they also have not been visible during their formation.

A record of a typical day's experiment is given in Fig. 1, when three sets of ergograms were taken at intervals of half an hour. For each ergogram there are recorded the total amount in kilogrammetres of work executed, the number of contractions, and the average height of the contractions, found by dividing the total height through which the weight is lifted by the number of contractions.

Investigations on muscular fatigue fall into two groups: those in which there is studied the fatigue of a single muscle,

or small group of muscles, so as to approach as nearly as possible to the mode of investigation of isolated muscle by purely physiological methods, and those in which there is studied the general fatigue produced by the activity of a large part of the musculature of the body. In this second line of investigation, in which so far very little has been done, the ergograph has been used as a test of the fatigue produced by such activities as walking, raising weights by turning handles, etc. These two kinds of investigation cannot be rigorously separated from one another; even in Mosso's method there must always be some activity of many muscles, not only that always present, but also that which is necessary to prevent general movements of the body. But such movements are small compared with the very heavy task given to the single muscle in this method.

The influence of drugs on general fatigue has also been studied by means of observations on large masses of men in campaigns, etc., but in such observations there is obviously involved much more than muscular fatigue. From the practical point of view the influence of drugs on such general activities are of much greater interest than the behaviour of an isolated muscle; but before the complex condition of general fatigue can be understood, it is necessary to study in as pure a form as possible the muscular fatigue and mental fatigue which form constituents of the complex condition, and in my own work I have only attempted to deal with these simpler problems.

Mental Fatigue.

One of the advantages of Mosso's method of studying muscular fatigue is that the subject is given a task which is so arduous that the element of fatigue greatly predominates over certain other factors which always come into play in some measure in studying the capacity for work. In the investigation of mental fatigue, on the other hand, the only exact methods hitherto used are such that the effect of fatigue is often masked by the presence of these additional features.

Nearly all the work on this subject comes from Kraepelin and his school, and it is also to this school that we owe most of our knowledge of the action of drugs on the capacity for mental work. In order to measure mental work some kind of unit is necessary, and to obtain such units only mental operations of a simple character can be employed. The units which have been most frequently employed are simple arithmetical operations, and the method most commonly used by Kraepelin and his followers is one in which the unit of work is that involved in the addition of two numbers. Kraepelin has drawn up books containing rows of figures, and his usual procedure in testing the influence of a drug on the capacity for mental work has been to ascertain the number of additions which can be performed in a given time, the time being divided into portions, so that a curve can be constructed showing the amount and rate of increase or decrease of work during the whole of the experiment.

Such a curve showing the results of an hour's work is due to the combined action of a number of different factors. In the great majority of individuals the curve rises for some time, though this rise is often broken soon after the beginning, and this rise is undoubtedly in the main due to the influence of practice. After a certain time the curve rises less steeply, and either passes into an approximately horizontal line, or may begin to fall, and this diminution of rise or actual fall is due in some measure to the occurrence of fatigue, though it is probable that in many experimental investigations loss of interest is also largely responsible. The initial rise is due, not only to practice, but also, and perhaps in large measure, to the influence of another factor, for which it is difficult to find a satisfactory term in English. Kraepelin has called it *Anregung*, and its equivalents in English are best given in the phrases 'warming to work' and 'getting into swing.'[1] It is the process by which the inertia of the psycho-physical machine is overcome. We all know how much this inertia

[1] Mr. Wimms has recently used the term 'incitation' as the equivalent of *Anregung* (*Brit. Journ. Psychol.*, 1907, vol. ii., p. 158).

may vary, and the degree of rapidity of this process of warming to work is a potent cause of irregularity in the form of the curve. Perhaps a still more important source of irregularity is given in the phenomenon of spurt. The work used in the experimental investigation of mental fatigue is always more or less monotonous, and there are apt to occur lapses of attention and application which are followed by spurts, and this phenomenon of spurt is especially pronounced at the beginning and end of a period of work.

The curve of mental work is, then, compounded of at least five factors, three—practice, warming to work, and spurt—tending to raise the curve, while the other two—fatigue and loss of interest—tend to depress it. The practical determination of the influence of such an agent as a drug on the process of fatigue is in consequence rendered a matter of the greatest difficulty. Much work and thought have been expended by Kraepelin and his school in the attempt to devise experimental procedures by which the conditions may be so varied as to provide data for the analysis of the curve of work into its various components.[1] The matter is one of the greatest difficulty, and little has yet been accomplished; but one advance has been made towards isolating the influence of fatigue. If periods of rest are given between periods of work, so as to allow recovery from fatigue, it is found that, other conditions being the same, some people require longer periods of rest than others, and the most favourable period of rest may be determined for each person, and the duration of this most favourable pause may be taken as a measure—rough, indeed—of the degree in which that person is susceptible to fatigue. This test, which has so far been applied chiefly to the study of individual differences, may also be used in studying the action of drugs on fatigue. By pauses of different lengths fatigue may be eliminated in different degrees, and the influence of a drug on this factor of the curve in some measure isolated.

[1] See 'Die Arbeitscurve,' Wundt's 'Philos. Studien,' 1902, Bd. xix., S. 459. In this paper Kraepelin describes an additional factor, *Gewöhnung*, or habituation, which he distinguishes from practice.

Apart, however, from any exact means of analysis, we shall probably not go far wrong in assuming that an earlier or steeper fall of the curve is due to increase of the part played by fatigue in the total effect, and, correspondingly, that a postponed or more gradual fall is due to a diminution of fatigue.

There is, however, one point of great theoretical interest to which I should like to refer briefly. In the earlier work of Kraepelin and his school, the problems connected with fatigue were studied by means of work carried on for long periods—for one or even for two hours. More recently it has been found that the effects of fatigue can be demonstrated even with such short periods of work as ten minutes. We know that if the work had been continued beyond the ten minutes, its amount would have steadily increased, perhaps for another half an hour or more, and the question is therefore raised whether the course of mental fatigue is properly represented by a curve which falls off at first slowly and then more rapidly. The mental work which has to be used experimentally is necessarily easy, and resembles the work of the dynamographic rather than that of the ergographic methods of measuring fatigue. We have seen that the former method shows the curve of fatigue to be one which falls off most rapidly at first, and then more slowly, till a constant level is reached, and the question arises whether this is not also true of the curve of mental fatigue.[1]

I have so far referred only to the quantity of work done in a given time as the measure of mental fatigue, meaning by quantity of work the number of units performed in a given time. It might be thought that the quality of the work would be even more important as a measure of fatigue; that with the onset of fatigue there would be a decided impairment of the correctness of the additions or other mental operations employed. As a matter of fact, it has been found—at any rate, in some cases[2]—that the number of errors is so small that they

[1] For further consideration of this question, see Appendix I.

[2] See Amberg, Kraepelin's 'Psychologische Arbeiten,' 1896, Bd. i., S. 336, and Rivers and Kraepelin, *ibid.*, Bd. i., S. 656.

are useless for the estimation of fatigue, and it is the custom to neglect the quality, and rely only on the quantity of the work. The possibility must not be forgotten, however, that in some cases the quality of the work may suffer from fatigue, and if in such a case the increase in quantity is accompanied by an impairment of quality, it may become extremely difficult to estimate satisfactorily the part played by fatigue.

Many objections have been brought against these methods of measuring mental work, both from the theoretical and practical points of view, and I must confine myself to two of them. All the methods employed in investigations of this kind are extremely laborious, and the work itself is monotonous and uninteresting, and it may be urged that we are measuring, not so much fatigue comparable to that resulting from bodily work, but rather the loss of interest due to the monotony of the occupation. There is much force in this objection, and some distinct experimental evidence might be adduced in support of it.[1] Nevertheless, it is found in practice that the work in question is far less monotonous than it would appear to be to those who have not tried it, this being largely due to the extrinsic interest given to the work by the scientific aim with which it is undertaken.

The other point is that the kind of work which has been chiefly used is so simple that, after a certain amount of practice has been gained, the work becomes almost automatic. This objection may be partly met by using mental operations of somewhat greater difficulty than those employed by Kraepelin; and in my own work with arithmetical methods I have used the task of multiplying four numbers mentally instead of the much easier task of adding two numbers, but even here, with practice, the operation tends to become very automatic.

Arithmetical operations are not the only means of studying

[1] Thus, Wimms has found (*op. cit.*) that, if the falling off in the amount of work is due to fatigue, fatigue must be greater with an easier than with a more difficult task.

the capacity for mental work, and I have also used type-writing, which has the advantage of being to most people more interesting than addition or multiplication, though there is the disadvantage that the task is more complex, involving as it does so much muscular as well as mental activity.

When we endeavour to compare the results obtained by the study of mental fatigue with those of muscular fatigue, we are met by the difficulty that the two kinds of fatigue have been studied by methods which have very little in common. Most of the work on muscular fatigue has been done by a method in which the task set is so great that fatigue, apparently complete, is induced in about a minute, while mental fatigue has been studied by methods in which the effects of fatigue may not be obvious, even at the end of an hour. This difference would probably be less striking if the dynamographic instead of the ergographic method were employed, but even here there is a very great difference in the magnitude of the task in the two cases. The methods of measuring mental fatigue differ radically in another respect from those used for muscular work, in that the means of measurement is by time rather than by the work itself. Fatigue is shown chiefly by alteration in the rapidity of work, while in the study of muscular work the rapidity is kept constant, and fatigue is measured by means of alterations in the actual amount of work of which the worker is capable.

Mr. McDougall has recently devised[1] a method of studying mental fatigue, or perhaps I should say, more precisely, fatigue of attention, which is in many ways more nearly comparable with the methods of measuring muscular work. An essential feature of the method is that stimuli are provided which may be called extrinsic. In the ordinary methods of studying mental activity, the stimulus to work comes wholly from within; the subject of the experiment has to keep himself working at the greatest rate possible, and it is a question whether the difficulty in ascertaining the existence of fatigue is not due to the occurrence of a kind of balance between

[1] *Brit. Journ. Psychol.*, 1905, vol. i., p. 435.

effort and accomplishment, in which work goes on at a more or less constant level, corresponding, perhaps, to the constant level of the dynamographic method of studying muscular fatigue.

In Mr. McDougall's method the subject is set the very simple task of hitting a succession of dots which pass before him through a slit. The rate at which the dots pass can be varied, and it is found that if they are made to pass at a speed which is near the maximal rate for the subject of the test, the onset of fatigue is rapid and obvious. It is a method in which fatigue is studied by means of the accuracy of aim—a method in which, in any one experiment, the rate of work is kept constant, as in the methods of studying muscular work, and the measure of fatigue is the quality of work.

In conjunction with Mr. McDougall, I have used this method to study the action of drugs; and other experiments recorded by Mr. McDougall show that the method is one well adapted for the study of their influence on mental fatigue.

In the instrument described by Mr. McDougall, and used by us, it was only possible to study the course of fatigue for a comparatively short time; but, with the aid of Mr. Horace Darwin, I have been able to devise a modification[1] by means of which the effects of fatigue can be studied for much longer periods. The completion of this apparatus has been, however, so long delayed that it has not yet been possible to carry out fully any observations with it on the action of drugs. I shall, however, be able to give the results obtained by Mr. McDougall and myself with the original apparatus.

The Action of Drugs.

Experiments on the action of drugs in fatigue may be carried out by two methods. In one method a certain amount of work is done every day for several periods, each of a week or fortnight, or longer. During some periods the drug is taken

[1] See Appendix II.

every day, but not at such a time of the day as to show its immediate effect on the work, while during other periods there is complete abstention from the drug. By this method there is tested the influence on the capacity for work of the general condition produced by the ingestion of the drug. No such work has hitherto been done on the capacity for muscular work; but it has been employed by Kraepelin and his school to test the influence on the capacity for mental work of alcohol taken daily for a certain period.

The other and more usual method by which the action of drugs is tested is to do a certain amount of work every day, taking a dose of the drug on some days and abstaining on other days. In this way, then, is tested not only the immediate action of the drug on the capacity for work, but by prolonging the work of each day the influence of the drug may be followed for many hours. This method is that which has usually been employed in the work I shall bring forward in these lectures.

The two methods could be combined; and this may be done most easily by comparing the work of the normal or control days during a drug experiment of the second class with the work of a similar series consisting wholly of normal days.

I have now described the general character of the methods which are employed in the study of muscular and mental fatigue, and can turn to the consideration of some aspects of the experimental study of fatigue which are of especial importance in estimating the influence of drugs.

We shall see later that the most varied methods have been used by different workers in studying the action of drugs. A common method has been to work to exhaustion, and then to see if the administration of a drug is able to call forth a further amount of work; others give a record of work which they state is their normal amount, and then give the result under the influence of a drug, but provide no indication of the relation between the supposed increment or decrement produced by the drug and the normal variations which occur from day to day.

The most satisfactory method, which was first adopted in a really systematic manner by Kraepelin, is to carry out work on a number of successive days (or days at regular intervals), keeping all conditions exactly alike on the different days, except that on some a drug is administered. The drug may be given before beginning the work of each day, but there are certain practical difficulties to which this procedure is subject. In many cases the drug-days will give an average which deviates from that of the normal days so greatly that there can be no question as to the action of the drug; but in other cases the deviation may be so slight that the question arises whether it may not be within the average deviation of the normal days from one another. There are, of course, definite methods for ascertaining the relation between a given difference and the probable difference due to normal variations, but their application in this branch of study is rendered very difficult by the existence of practice, etc.—*i.e.*, we have to do not merely with a number of days which differ from one another by chance variations of daily disposition, etc., but with days which differ owing to the existence of certain more or less regular influences which, though they no doubt follow definite laws, are not yet sufficiently understood to allow the application of statistical measures.

This difficulty may, however, be overcome in large measure if the drug is given at some period after the work has been begun, so that the results can be expressed in relation to the initial performance before the drug has been taken. This latter method is that which I have usually employed.

In carrying out an experiment of this kind, extending over a number of days, it is essential that all the conditions of life be kept as constant as possible. The same amount of sleep must be taken every night, the meals must be of the same kind and at the same times every day, the same amount of exercise must be taken, and the same amount of other work done. To do experimental work of this kind really satisfactorily means to most people that they must cut themselves off from many of the ordinary pursuits of life so long as the experi-

ments last. In my own case the fact that my occupation involves very different amounts of work on different days has made it impossible, as a general rule, to carry out any experimental work during term-time, and my own most satisfactory work has been done in the country, away from all possible sources of disturbance.

In the case of muscular work, the necessity for rigorous equality of the conditions of life is perhaps not so great as in the case of mental work; but here the more similar the conditions can be kept, the more likely is it that satisfactory results will be obtained.

It must be understood that these rigorous conditions are not necessary for the crude determination of the action of large doses of drugs; but it is not with such work that I am now concerned. It is my object in these lectures to consider the methods to be followed in the endeavour to ascertain the effects of those doses of drugs which are used either for dietetical or therapeutical purposes, and for such an object unequivocal results can only be expected if the conditions of life are kept as rigorously uniform as possible.

A difficulty which arises in drug experiments is due to the practice of taking as part of the normal diet substances which have an effect on the capacity for work; and this difficulty becomes especially great when it is one of these drugs which is the subject of experiment. There are two possible lines of action: the use of the substances may be wholly discontinued before the experiment begins, or the experimenter may continue to take them, but in exactly the same quantity every day and at exactly the same times, while he may perhaps diminish their amounts. The former procedure, which has been adopted by several workers, is open to a serious danger, to which my attention was called by my own experience. I began my work on drugs with an experiment on the effects of caffeine, and discontinued the use of tea and coffee shortly before the experiment began, having previously taken them in diminished quantity. The act of giving up the use of these substances was followed by loss

of energy, which greatly interfered with the success of the experiment, and a later repetition of the experience left little doubt that the condition was due, at any rate in part, to the discontinuance of the use of tea and coffee. My reaction was probably exceptional; but a condition which is so pronounced in one person is probably present to some extent in all, though it may be masked by other variations in bodily and mental health. Indeed, it seems only natural that the sudden cessation of the habitual action of such a substance as caffeine must have a decided effect on those vital processes on which it has any influence.

If, in investigations on the effect of such a substance as alcohol in one accustomed to it, the use of the active substance is only given up shortly before the commencement of the experiments, there is a further danger. Even in those who only take such a substance in moderate amounts, its disuse is probably followed in some degree by the craving which is so pronounced after discontinuance of large amounts, and, slight and hardly noticeable as this craving may be, it may yet be sufficient to produce an obvious effect when the article of which the person has been deprived is administered experimentally. The effect of the substance given experimentally may be the result, not of its normal physiological action, but of the satisfaction of a craving. For these reasons it seemed best to give up completely the use of all the stimulating articles of diet in ordinary use for several months before beginning my next research, and much of the work to be described in these lectures was done more than a year after the use of alcohol and caffeine-containing articles of diet had been given up, except for experimental purposes or on such rare occasions that there could be no question of habituation. So drastic a procedure is not likely to attract workers to this subject; and though it has been followed also by Mr. Webber, who has been my co-worker in many of the researches to be described in these lectures, I have been content in other cases to allow the continued use of tea, coffee, alcohol, or tobacco, but in equal amounts and at the same times every day, and

wherever possible not till after the experimental work of the day has been done.

Another difficulty arises in connexion with practice and training. Some recent workers have insisted on the necessity for long-continued training before beginning to use ergographic curves as objects for scientific study, and one, Hellsten, trained for many months before he began to study the action of drugs.

By following such a rule it seems to me that a great experimental opportunity is being neglected. One of the features of the work of untrained muscle is the occurrence of painful or unpleasant sensations ; and since one of the definite problems in connexion with the effect of drugs on fatigue is how far they act through their influence on the sensations of fatigue, comparative work on trained and untrained muscle may be of great value. In my own work, therefore, I have tested the influence of drugs in various conditions of training, and in every case introspective notes have been recorded to show whether painful or other unpleasant sensations have been experienced during the course of the experiment.

I can now pass to a feature of method in which lies the chief interest of the new work I hope to bring before you—a feature designed to eliminate the influence of certain psychical factors which have undoubtedly been allowed to affect the results of nearly all who have experimented on the action of drugs. Many of these workers have considered the possibility that their results may have been influenced by suggestion, or of bias towards results which were to be expected theoretically, and some have shown that effects similar to those following the administration of a drug may be the consequence of the administration of a wholly inactive substance which is supposed by the subject to be the drug in question. Few, however, have adopted the obvious precautions which such considerations suggest ; Schumburg[1] and

[1] *Arch. f. Anat. u. Physiol.*, Physiol. Abth., Suppl. Bd., 1899, S. 289.

Sobieranski[1] are the only workers with drugs[2] who have used any kind of control-substances, and even they do not make it clear that the control mixtures or injections they used were entirely indistinguishable from those containing the active substances.

The factor which previous writers have considered under the title of 'suggestion' is far from being the only source of error in work on the action of drugs. Féré has shown that the sensory stimulation involved in the act of taking a drug into the mouth and swallowing it may have a very decided effect on the amount of work executed with the ergograph, but even this knowledge did not lead him to adopt any control in his numerous researches on drugs.

There is, however, another factor which is probably more important than either sensory stimulation or suggestion—viz., the interest and excitement produced by taking a substance when the discovery of its effect is the motive of the whole experiment. The ergographic curve is an extremely delicate reagent to any form of mental excitement. Any novelty in the course of an experiment may have a very decided effect on the amount of work. The interest of a conversation, the knowledge that the performance is being watched, the view of the weight rising as one works or of the formation of the ergogram on the drum, or any other variation in the routine of the daily experiment, may have very obvious effects on the amount of work. Similarly, the knowledge that it is the first or last day of an experiment may produce a distinct increase in the amount of work, so decided that I now always adopt the procedure of working for one or two days before and after the period which is to provide the proper data for the experiment.

If such a condition of interest as that arising from its

[1] *Centralbl. f. Physiol.*, 1896, Bd. x., S. 126.

[2] Schumburg has also used dulcin as a control substance in work on the action of sugar (*Zeitschr. f. diätetisch. u. physikal. Therapie*, 1899, Bd. ii., S. 185), and irreproachable work from this point of view has been done by Pregl (*Arch. f. d. ges. Physiol.*, 1896, Bd. lxii., S. 379) on the action of orchitic extract.

being the first or last day of an experiment, or that resulting from the view of the weight rising as the finger contracts, can have very appreciable effects on the amount of work, it is clear that so interesting an occurrence as the administration of a drug must have a decided influence, and the interest so aroused will probably be equally great whether the nature of the drug is unknown, so that there is an element of mystery in the occurrence, or whether its nature is known. When in the latter case the subject is himself the experimenter, keenly interested in the possible results of his experiment, this factor of interest must often be very strong.

In my first experiment with a drug, I soon became aware of the existence of such interest. I noticed that the days on which I took the drug interested me more than the normal days on which nothing was taken. I felt at once stimulated by the fact of having taken the substance, the action of which I was trying to test, and it was obvious that I had no means of telling whether any effect which might be produced was due to this interest or to the proper physiological action of the drug. In all future experiments I therefore determined to endeavour to disguise the days on which the drug was being taken and all the new work to be described in these lectures has been carried out with the use of control mixtures which have usually been wholly indistinguishable from those containing the active substances. The subject of an experiment has taken every day at some time in its course a dose of a mixture, and has been wholly unaware whether he has taken the substance which is the motive of the experiment or some inactive imitation of it. These control mixtures have in most cases been prepared for me by Dr. W. E. Dixon, to whose help in this direction I am very greatly indebted. In some cases in which I have myself been the subject of the experiment, Dr. Dixon has given me two or more bottles, and it has only been at the end of the experiment that I have been made acquainted with the exact nature of their contents.

My own work has been chiefly on caffeine and alcohol,

and with the former of these we were rapidly successful in disguising the taste. We used citrate of caffeine, and an indistinguishable control mixture was made of gentian and citric acid. With alcohol we had greater difficulty; but the consideration of this may be deferred till I come to deal with the work on that substance.

I have not myself experimented with subcutaneous injections of any drug, but it is obvious that control injections are in such a case just as necessary as are control mixtures when the drug is given by the mouth.

Most of those who have written on the action of drugs on the capacity for work have not distinguished definitely between the action on the pure capacity for work in the unfatigued condition and the action on the process of fatigue, with which we have especially to do in these lectures. A complete distinction of this kind is, perhaps, impossible, for it is probable that the fatigue process comes into play from the first moment of beginning to work; but, nevertheless, the distinction can be made in practice to a great extent, and I shall endeavour to make it, not only in the account of my own work, but also in that of the work of others, even when it has not been made by the authors themselves.

The method which I have adopted of recording sets of ergograms separated by intervals of rest is particularly adapted to bring out the distinction in question, and we shall see that there is evidence that the effect of a drug may be different at the beginning of a set of ergograms from that shown as the set is continued.

LECTURE II

CAFFEINE

Action of caffeine on muscular fatigue; historical; new experiments with ergograph; twofold nature of action of caffeine—Action on mental fatigue; historical; new experiments with typewriting and by McDougall's method; slightness of stimulating action.

I WILL begin my survey of the work which has been done on the action of drugs in fatigue by taking up the group of substances of which caffeine is the most important constituent. These substances are in habitual use as stimulants of work, and I may as well say at once that their universal reputation is not belied by the results of experiment.

In the earliest work on muscular fatigue the dynamometer was used. In 1892 De-Sarlo and Bernardini[1] found that caffeine produced a slight increase in the force of the contractions with this instrument, and Kraepelin[2] found tea to have the same effect.

Since that time most workers have used the ergograph of Mosso, either in its original form or in one of its modifications. In 1893 Ugolino Mosso[3] used it in his work on the action of kola, which he found to have a highly stimulating effect, the work done in a single ergogram being increased fourfold, this action being due chiefly to the caffeine which the kola contained.

In 1894 Koch[4] tested the action of a dose of caffeine taken when the muscles had already been exhausted, and found that

[1] *Rivista sper. di Freniatria*, 1892, vol. xviii., p. 1.

[2] 'Ueber die Beeinflussung einfacher psychischer Vorgänge durch einige Arzneimittel,' Jena, 1892, S. 143.

[3] *Arch. ital. de Biol.*, 1893, t. xix., p. 241.

[4] Inaug. Diss., Marburg, 1894.

they were rendered capable of continued activity. His work is notable for the demonstration that a great increase in the amount of work executed with the ergograph can be produced by suggestion, but Koch found that the increase produced by caffeine exceeded that which could ever be produced by this means.

In 1894 Rossi[1] found only a slight increase in the amount of work under the influence of caffeine, the effect being due to increase in the number of the contractions.

In 1896 Sobieranski[2] tested the influence of caffeine, not only on the capacity for voluntary work, but also when the contractions were produced by electrical stimulation of the muscle, and found an increase by both methods, the effect of the drug being produced more slowly with electrical stimulation; and, in spite of the well-known fact that caffeine stimulates muscle directly, he concluded that its effect in man is chiefly through its central action.

In 1896 was published the important work of Hoch and Kraepelin[3] on the action of the constituents of tea on the capacity for muscular work. An improved form of Mosso's ergograph was used, in which the movements were strictly limited to one joint, and other disturbing features of the earlier instrument were remedied. In three subjects ergograms were taken, at intervals of ten minutes, for an hour after the administration of caffeine, the essential oils of tea, and maté. The caffeine was found to increase the amount of work, while the oils produced a decrease; maté produced an increase which was on the whole less pronounced than that due to the caffeine.

Hoch and Kraepelin paid especial attention to the respective influence on the number of the contractions and on their average height, and found that the action of caffeine is predominantly on the latter, although their figures show that there is often also an obvious effect on the number. The interval

[1] *Rivista sper. di Freniatria*, 1894, vol. xx., p. 458.
[2] *Centralbl. f. Physiol.*, 1896, Bd. x., S. 126.
[3] Kraepelin's 'Psychologische Arbeiten,' 1896, Bd. i., S. 378.

of ten minutes allowed between successive ergograms is long enough in many persons to allow a large amount of recovery from the fatigue produced by an ergogram, and in a fourth subject who recorded ergograms at intervals of only five minutes the effect of caffeine was much less pronounced.

The interest of some work published by Tavernari[1] in 1897 arises from the fact that he tested the influence of coffee on ergographic work, when in a state of general fatigue induced by a walk of thirty kilometres, and found little influence.

In the same year Destrée[2] records a stimulating action of caffeine, but only in a slight degree.

The next work is by Benedicenti,[3] who worked with coffee, tea, maté, and guarana, but did not use caffeine in a pure form. With each substance he found an increase in the work of a single ergogram, the effect of the coffee being especially to prolong the ergogram, thus disagreeing with Hoch and Kraepelin, who believe the effect to be chiefly on the heights of the contractions.

The work by Schumburg,[4] published in the same year, is more important. This worker used a control, though it is not clear that his subjects were unable to distinguish between the active and the control substances. On some days Schumburg tested the action of kola, coffee, tea, or caffeine on the work recorded in a series of ergograms; on other days the experiment was complicated by the addition of work, in which general fatigue was produced by means of the ergostat, an instrument in which a weight is lifted by turning a handle, and Schumburg used this instrument till either 18,000 or 21,600 kilogrammetres of work had been done. Kola produced an increase in the ergographic work both with and without general fatigue, but the caffeine only increased the uncomplicated work with the ergograph, and even seems to have had a depressing effect on the work done in the

[1] *Rivista sper. di Freniatria*, 1897, vol. xxiii., p. 102.
[2] *Journ. méd. de Bruxelles*, 1897.
[3] Moleschott's 'Untersuch.,' 1899, Bd. xvi., S. 170.
[4] *Arch. f. Anat. u. Physiol.*, Physiol. Abth., Suppl. Bd., 1899, S. 289.

presence of general fatigue, but only few experiments of this kind were made.

Schumburg's work is interesting from a point of view of method, in that he endeavoured to determine whether the drug exerted its action chiefly on that portion of the ergogram recorded without special effort, or on that portion recorded only after such special effort had begun to be necessary, but with no very decisive result.

In 1901 Féré[1] came to the conclusion that coffee, caffeine, and theobromine acted merely as accelerators of fatigue, this result being produced when the coffee was swallowed in such a way as to exclude any effect due to stimulation of taste.

In the same year, Oseretzkowsky and Kraepelin[2] published observations in which doses of 0·5 gramme of caffeine were found to have no appreciable effect on the amount of work, increasing the heights of the contractions to some extent, but at the same time diminishing their number. In this case the ergograms were taken at intervals of only two minutes, so that the element of fatigue would have played a greater part than in the work of Hoch.

The most recent papers on caffeine are those of Hellsten[3] and Joteyko,[4] both published in 1904. The former used a new form of ergograph, in which both arms are used, so that about 6,000 kilogrammetres of work are done during the performance of one ergogram, instead of the 4 to 8 kilogrammetres usual with Mosso's instrument. Tea was found to have only a slight effect.

Mlle. Joteyko's work is chiefly interesting as a record of her attempt to draw conclusions from the mathematical analysis of the ergographic curve. She believes that this curve can be analysed into three component curves, one rising as the square of the time which she believes to repre-

[1] *C. R. de la Soc. de Biol.*, Paris, 1901, pp. 593 and 627. See also 'Travail et Plaisir,' Paris, 1904, p. 311.

[2] 'Psychologische Arbeiten,' 1901, Bd. iii., S. 617.

[3] *Skand. Arch. f. Physiol.*, 1904, Bd. xvi., S. 197.

[4] 'Travaux du Laboratoire de Physiologie,' Instituts Solvay, Bruxelles, 1904, t. vi., p. 361.

sent the process going on in the central nervous system during the performance of the work. The other constituent curves run a descending course : one, which falls directly as the time, is believed to represent the consumption of material in the muscle ; while the other, which falls as the cube of the time, is believed to represent the process of poisoning of the muscle by the products of activity. Three-quarters of an hour after taking a dose of caffeine it was found that the parameters of all three curves had increased, and this is ascribed to an exciting action on the central nervous system, which leads to more rapid consumption of material and more rapid accumulation of the poisonous products of activity. An hour and a half after taking the drug, on the other hand, the three parameters had diminished, and this is ascribed to a depressing action on the central nervous system, with consequent slower consumption of material and accumulation of metabolites.

These conclusions of Mlle. Joteyko are based on the changes which take place in the form of the individual ergogram. In my own work with the very much improved form of Mosso's ergograph devised by Kraepelin, the form of the ergogram is singularly constant, and nearly all conform to the same general type, not only in the same person under different conditions, but also in different persons. It becomes a question how far the changes in the form of the ergogram described and analysed by Mlle. Joteyko are due to her ergograph allowing other muscles to come into play as the muscle originally used became fatigued.

This review of previous work shows a general agreement as to the stimulating influence of caffeine on the capacity for muscular work, though different workers are not agreed upon the exact way in which the drug affects the ergogram, and have found great differences in the degree of its potency. Some of these differences are doubtless to be referred to differences of susceptibility of the subjects of the experiments, but others are probably due to differences of method, and

others, again, to different degrees in which the factor of fatigue has been of influence.

My own observations have been made on two persons only, Mr. H. N. Webber and myself, who will often be referred to as W. and R. respectively. Mr. Webber's experiments have been not only more numerous, but more satisfactory, than my own. This is due to several causes. In the first place, he could give his whole time to the work, so that he was able to keep his daily occupations almost completely uniform.

In my own case, on the other hand, lectures and other engagements made it impossible to keep different days on the same level of general activity, and I was obliged to limit my work to vacations, and even here other work, from which I could not escape, often made it impossible to keep the total mental activity of a day on as uniform a level as was possible in Mr. Webber's case. In the second place, I was very much troubled throughout my ergographic work by muscular pain. I required long-continued practice, gradually increasing the amount of work done day by day, before I could carry out series of ergograms of the length desired. I shall therefore deal first with the work done by Mr. Webber.

Experiments of the Subject W.

Experiment 1.—In this experiment, which lasted for eight days, three sets, each of six ergograms, were recorded, beginning on each day half an hour after a light breakfast. The right and left hands were used on alternate days. The weight lifted was 4·5 kilogrammes; the interval between the successive ergograms of a set was two minutes, and that between the successive lifts of each ergogram two seconds, the finger being flexed with one beat and relaxed with the next beat of a metronome beating seconds. Between the sets there was an interval of half an hour, which was occupied in attending to the apparatus while the other subject was performing an experiment, so that the arms were gently

exercised and there was a certain amount of mental occupation of an unfatiguing kind.

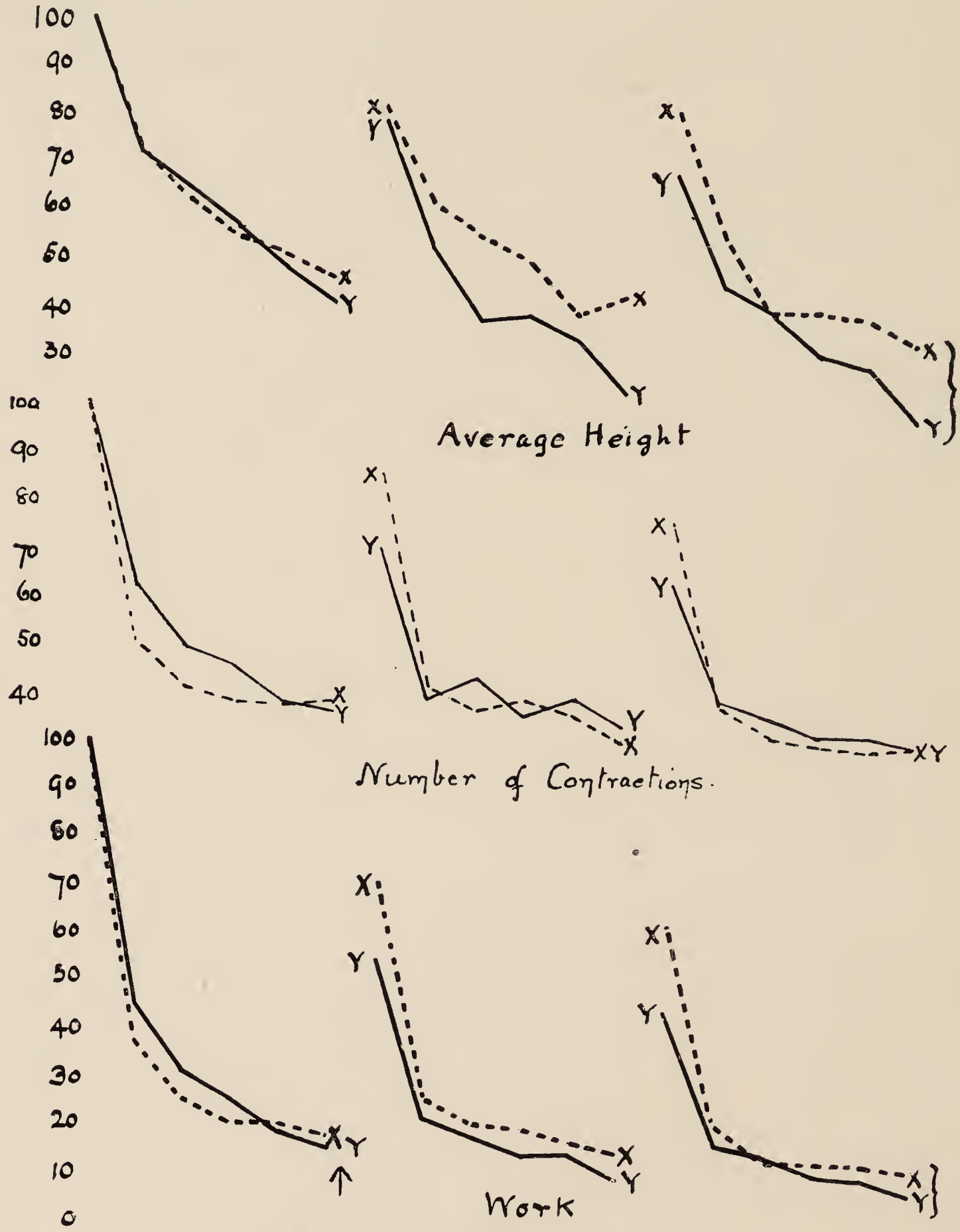

FIG. 2.—CAFFEINE EXPERIMENT W. I.

X, Caffeine citrate, 0·3 gramme. Y, Control mixture. Arrow shows when the dose was administered.

The caffeine was taken in the form of the citrate, and the control consisted of a mixture of gentian and citric acid. The dose, whether of caffeine or control, was taken ten minutes

before beginning the second set of ergograms, and in this, as in all the caffeine experiments, the disguise was complete, so that the taste gave no indication whether a day was one on which the effect of caffeine was being tested or was one of the normal days.

The general results of this experiment are shown graphically[1] in Fig. 2, in which the data for the ergograms of the three sets are expressed as percentages of those of the first ergogram of the first set. The curves in the lower part of the figure represent the course of the work executed in the successive ergograms, those in the middle of the table the course taken by the number of contractions, and those at the top of the table that of the height of the contractions, found by dividing the total height through which the weight was lifted by the number of contractions. The curves marked X show the course of the caffeine days, and those marked Y that of the days on which only the control mixture was taken.

As the dose, whether of caffeine or control mixture, was not taken till the interval between the first and second sets, the work of the first set was done under the same conditions on the two groups of days, and the two curves should show a close correspondence.

The actual correspondence is very close. In the case of the curve for work, the caffeine days show at first a slight falling off as compared with the normal days, followed by a slight rise ; but these differences, dependent on the inevitable variations from day to day, are very slight, and the closeness of the correspondence may be taken as evidence that the general conditions of the experiment were satisfactory. The work of the second set of ergograms, begun ten minutes after taking the dose, seems to show a drug-effect ; for, though the caffeine curve is not much above the normal curve, it is so throughout, and nowhere falls to the level of the latter. The increase is most decided in the case of the first ergogram of the set, where the work of the average ergogram on the

[1] For the figures on which these and the succeeding curves are based, see *Journ. Physiol.*, 1907, vol. xxxvi., p. 33.

caffeine days is 71 per cent. of the initial performance, while that of the normal days is only 54 per cent. In the third set, begun fifty-five minutes after taking the dose, the same decided increase is shown in the first ergogram, the amounts being 61 per cent. and 42 per cent. respectively; but the increase throughout is not so constant as in the second set, the third ergogram on the caffeine days falling a little below that of the control days.

The effect of the caffeine comes out more obviously in the figures for the total work of the sets. Since the dose was not given till the end of the first set, the total work of this set may be taken as a normal standard; and if it be taken as 100, the amount of work for the second and third sets comes out at 74 per cent. and 55 per cent. on the caffeine days, as compared with 56 per cent. and 42 per cent. on the normal days. The constancy of the difference between the work curves for the caffeine and control days justifies the conclusion that these data show a real, though not a very pronounced, effect of the drug; for if the differences had been due to chance variations, the relations between the two curves would probably have been less regular. The effect, however, is evidently slight, and is of an order quantitatively very different from that found by some earlier workers.

The curves for height and number of contractions given in Fig. 2 show that the effect on the work of the first ergogram of each set is chiefly due to an increase in the number of the contractions, while the effect throughout the whole course of the sets shows itself chiefly in increase of their height.

It may be noted that this experiment was carried out in an early condition of training, as will be very evident from the sample of the ergograms of the left hand, given in Fig. 3, A. The irregularity of the ergograms, especially towards the end of the set, is very great, and presents a very striking contrast with the ergograms (Fig. 3, B) of the same worker a few months later.

Experiment 2.—This experiment, carried out six months later, was conducted on the same general lines as the first

experiment, but with several important differences. In order to follow the effect of the drug for a longer time, five sets of ergograms were recorded. To the end of the third set the intervals were half an hour, as in the earlier experiment; but the two remaining sets were taken at intervals of an hour, so that the total duration of the experiment of each day was four and a quarter hours, and the dose being taken, as in the first experiment, ten minutes before the beginning of the second set, the effect of the drug was followed for over three

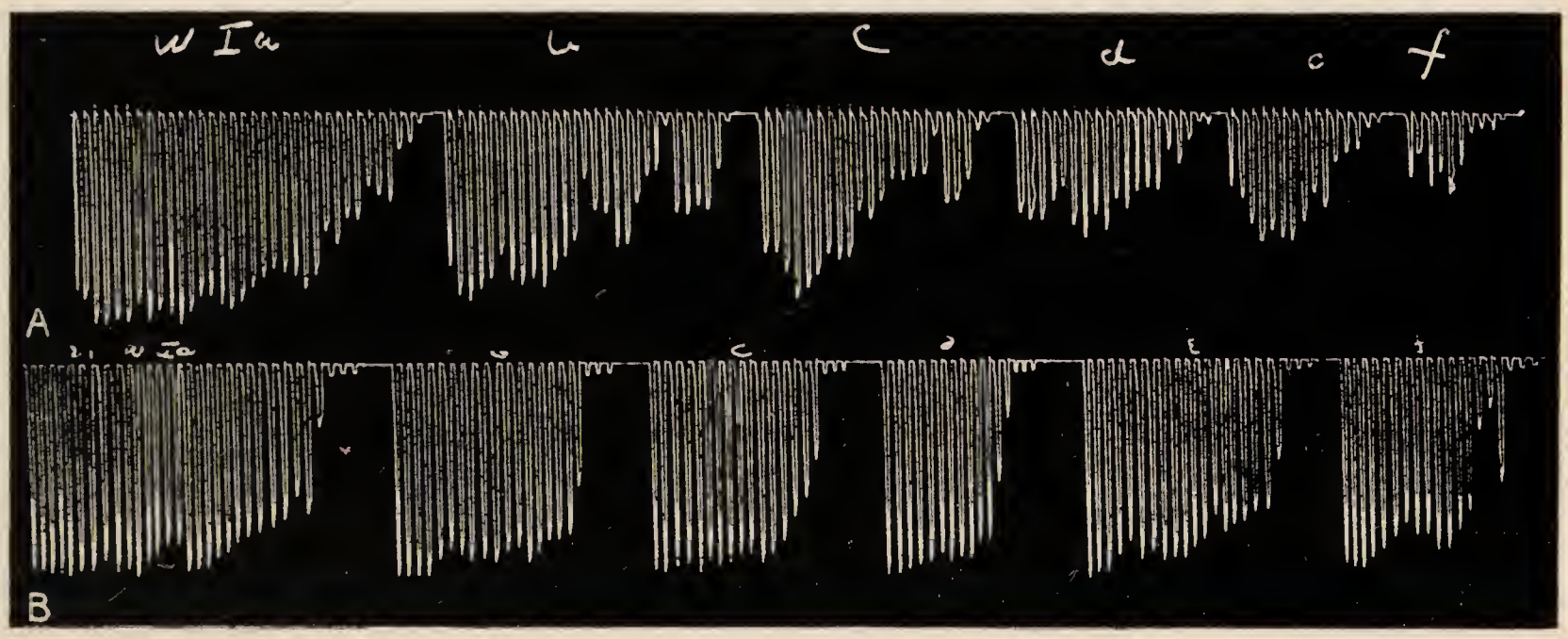

Fig. 3.

and a half hours. The intervals were occupied in the same way every day, In the first two intervals light work was done in connexion with tracings (cutting them up, pasting them in a book, etc.); the third interval was passed in light reading and a few biscuits were eaten; the fourth interval was occupied in making calculations of percentages—*i.e.*, in mental work of a tedious, but not arduous, character. A second difference was that the dose was increased from 0·3 to 0·5 gramme. A third and very important difference was connected with the condition of training. During the intervening months a number of experiments had been carried out by the subject to test the influence of alcohol in which the left hand had been exclusively used. In consequence, the left arm was by this time in a very completely trained

condition, while the right hand had had no more training than in the previous experiment.

Owing to the prolonged training of the left hand, the distance through which the weight of 4·5 kilogrammes was lifted in the largest ergograms so nearly approached the available height of the scale that the weight for this hand had to

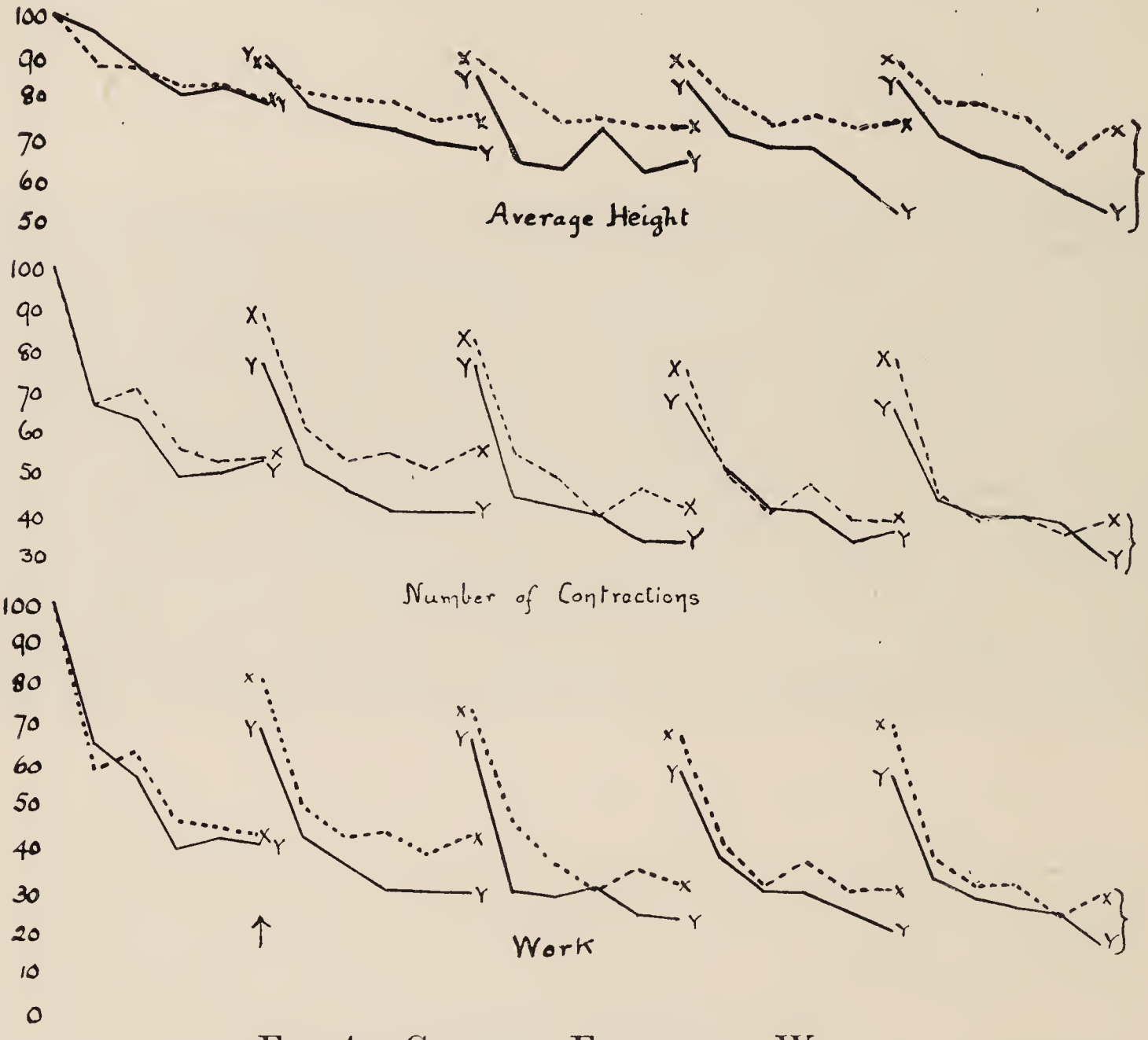

FIG. 4.—CAFFEINE EXPERIMENT W. II.

X, Caffeine citrate, 0·5 gramme. Y, Control mixture. Weight: right hand, 4·5 kilogrammes; left hand, 5·0 kilogrammes.

be increased to 5 kilogrammes, but that for the right hand was 4·5 kilogrammes, as in the earlier experiment.

The results are given in Fig. 4, constructed on exactly the same plan as Fig. 2. It will be seen that there is a very close correspondence in the general features of the two groups of curves. The curves for the first set, taken before any dose had been administered, show a very satisfactory correspon-

dence, while in all the sets taken after the dose the caffeine curves for the amount of work are above the normal curves, except for one ergogram in the third set and another in the last set. The first ergogram of each set on the caffeine days is distinctly larger than that on the normal days, but the predominance of the effect at the beginning of the sets is not as pronounced as in the first experiment. The constancy of the increase and the close correspondence of the curves for the two experiments can leave little doubt that we have to do with a real effect of the drug.

The correspondence with the results of the first experiments comes out also very strongly on comparing the curves for the number and height of the contractions. Except in the second set, the increase in the number of contractions is only decided in the first ergogram of each set, while the effect throughout the whole course of the sets is predominantly on the heights; and this effect on the heights is very decided, the irregularities of the curves for work being seen to be due to fluctuations of the number of the contractions. This agreement in the details of the results of the two experiments lends further support to the conclusion that we have to do in both experiments with a real effect of the drug.

In the preceding curves the results for the two hands have been grouped together; but there was some difference in the amount of increase on the two sides, the effect being in each case most pronounced on the right side.

Experiments of the Subject R.

In my own earlier experiments it was not possible to record sets of six ergograms, owing to the fact that so large a number produced such muscular pain as to render further continuance of the experiment impossible. After several fruitless attempts, an experiment of four days was carried out on March 1 to 5, 1906 (omitting March 4), in which three sets of ergograms were taken; but each consisted of four ergograms only, two taken with each hand. In other respects the conditions of the experiment were exactly the

same as in the first experiment of W., the dose of caffeine being 0·3 gramme, taken ten minutes before the beginning of the second set. Even in this experiment several ergograms were brought to a premature conclusion by pain, and owing to this incompleteness, it is sufficient to record that, while on the normal days the total work of the second and third sets, as compared with the first set, decreased by 25 and 16·7 per cent. respectively, the work of the second set on the caffeine days only decreased by 3·2 per cent., while the work of the third set increased to the extent of 16·4 per cent.

Experiment 2.—This experiment, with the same dose, lasted for eight days (March 6 to 8 and March 12 to 16), on four of which the contractions of the finger were carried out in the usual manner (see Fig. 5, A), while on the other four days each contraction was only allowed to reach two-thirds of its usual extent (see Fig. 5, B), by means of an obstacle placed in the way of the moving finger. In this experiment, as in the first, only two ergograms were executed with each hand in each set, and the course of the effect of caffeine could be represented for so short a time that I do not give curves showing the figures for each ergogram, but have grouped the results of each set together in the following table :

Complete Contractions.

		First Set.	Second Set.	Third Set.
Work (in kgm.) ...	Caffeine	6·8 (100)	7·6 (112)	8·5 (125)
	Control	7·8 (100)	7·1 (92)	6·1 (78)
Number of contractions	Caffeine	45 (100)	49 (109)	55 (123)
	Control	49 (100)	49 (99)	43 (85)
Average height (in cm.)	Caffeine	3.4 (100)	3·5 (101)	3·4 (100)
	Control	3.5 (100)	3·2 (91)	3·2 (91)

Incomplete Contractions.

Work	Caffeine	5·2 (100)	6·7 (130)	6·6 (126)
	Control	5·9 (100)	5·8 (99)	5·5 (94)
Number of contractions	Caffeine	51 (100)	65 (131)	64 (128)
	Control	58 (100)	59 (101)	55 (96)

In the case of both complete and incomplete contractions it will be seen that there was a very decided caffeine-effect—so decided as to be beyond all doubt. In the case of the

complete contractions, the amount of work on the caffeine days increased by 25 per cent., while on the control days it fell off to the extent of 22 per cent., this increase on the caffeine days being due pre-eminently to increase in the number of the contractions, though there was also an effect on the height, for this remained level instead of decreasing, as on the control days.

In the case of the incomplete contractions, the effect of the caffeine is not so pronounced, and is more decided in the second than in the third set of ergograms. The figures for

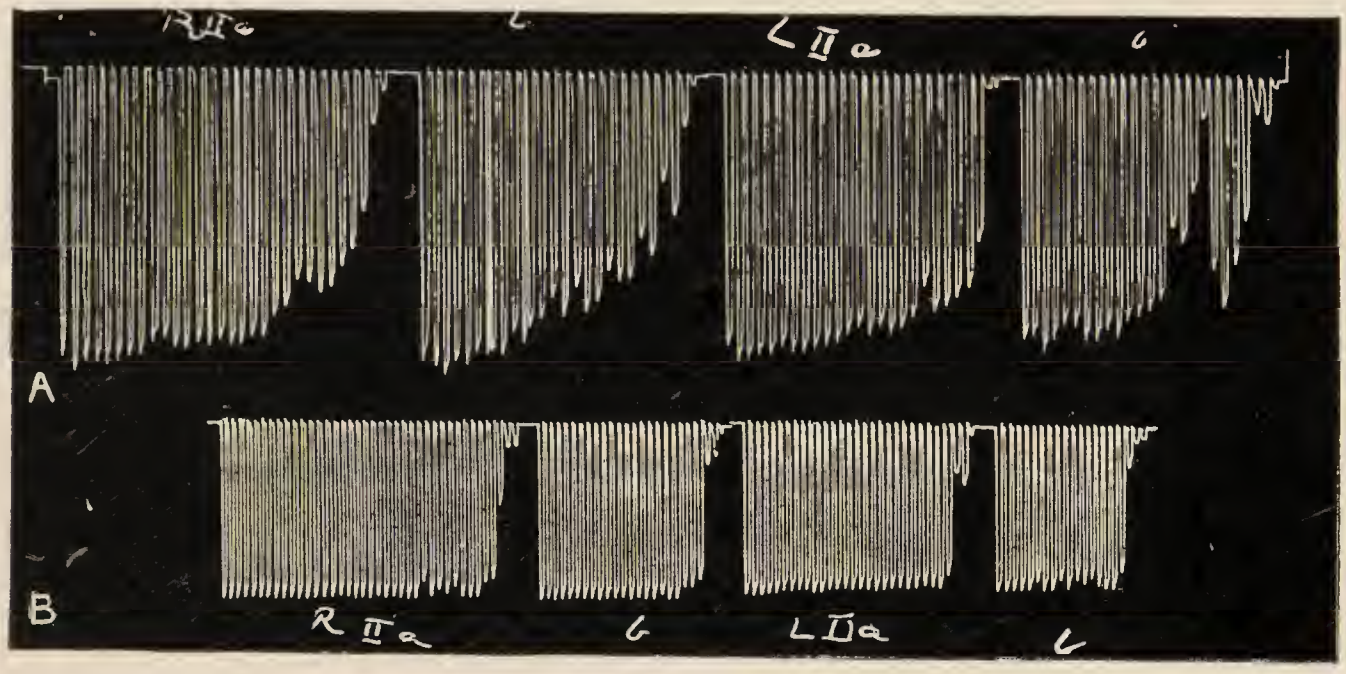

Fig. 5.

the normal days show that the fatigue produced by one set of ergograms was less than with complete contractions, the work only falling off to the extent of 6 per cent., instead of 22 per cent., as with the complete contractions.

Experiment 3.—Six months later a third experiment with caffeine was carried out by the same subject. By this time he had undergone so prolonged a training, chiefly in connexion with work on the effect of alcohol, that he was able to perform an experiment in which the work of each day consisted of five sets, each of six ergograms, so that the work is exactly comparable with that of W., except that only one hand—the right—was used. The dose of caffeine was the same as that taken by W. in his second experiment—viz., 0·5 gramme. The experiment was designed to last for eight

days; but at the end of six days it was found that the dose of caffeine, though taken in the middle of the day, was disturbing the sleep of the subject at night,[1] and the experiment was therefore discontinued.

The results of the experiment are shown graphically in Fig. 6, arranged on the same plan as in previous figures. It

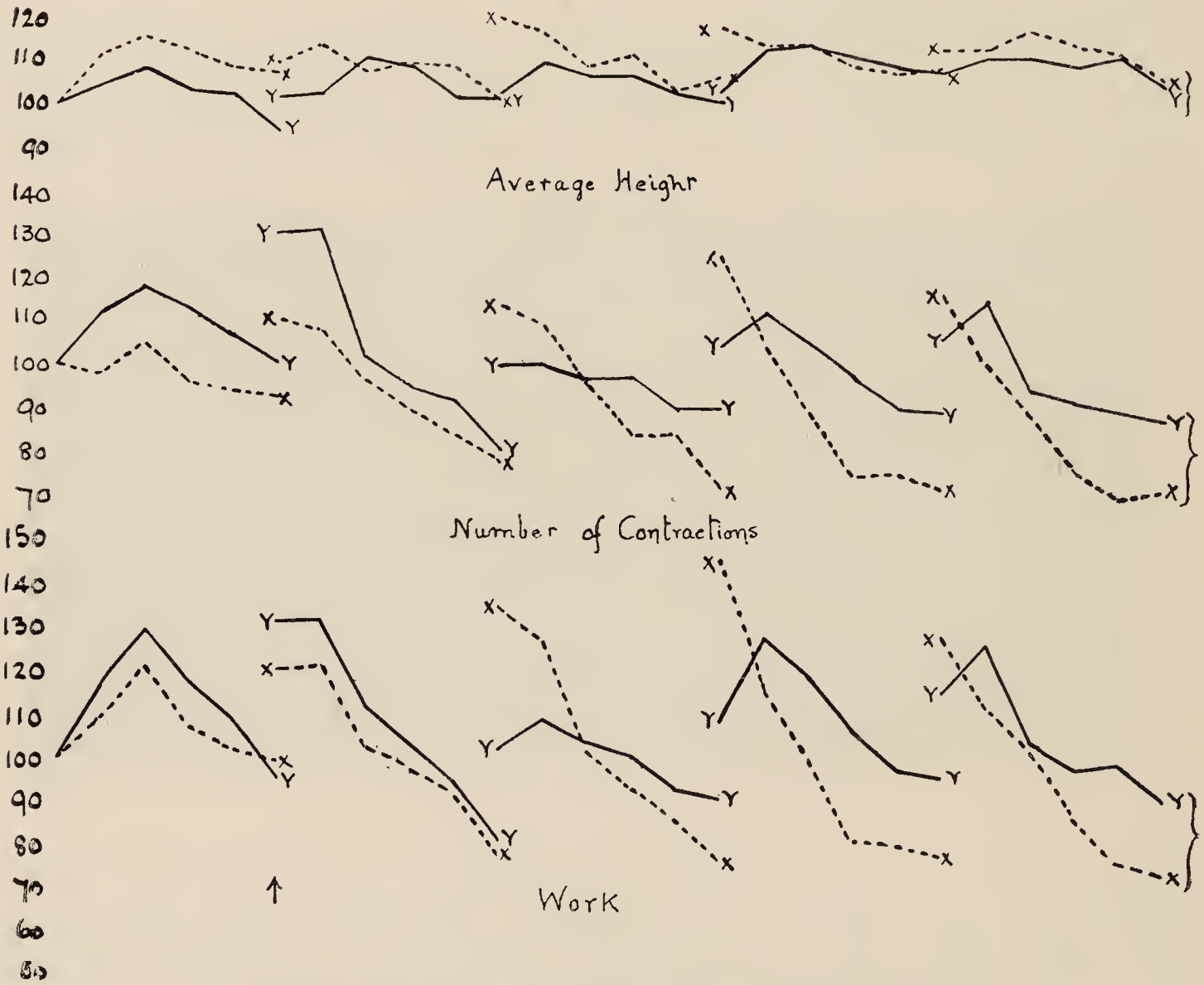

FIG. 6.—CAFFEINE EXPERIMENT R. III.
X, Caffeine citrate, 0·5 gramme. Y, Control mixture.

will be seen that the caffeine and normal curves of the first set, recorded before the dose was taken, show a very fair correspondence, and that the curves of the second set, begun ten minutes after taking the dose, show no indication of a caffeine-effect, the work falling somewhat below that of the normal days. In the succeeding sets there is, however, a very pronounced effect, of a kind very different from that of the subject W. The first two ergograms of the third set

[1] See Appendix III.

show a great increase, as compared with the control days, and then the remaining ergograms of the set fall decidedly below those of the normal days. At the beginning of the fourth set, an hour later, the stimulating effect of caffeine is very pronounced; but it disappears even earlier than in the third set, and the curve falls still more below the normal level. In the last set there is the same kind of effect, though the initial increment and later fall are not so great.

In these observations, the course of the first set of six ergograms is not so regular as in the case of W., and as it seemed possible that the expedient of expressing the results in percentages of the first ergogram might be unsatisfactory, and give an untrue picture of the course of the fatigue and of the drug-effect, the curves have been worked out in a different way, the results being expressed as percentages of the average ergogram of the whole of the first set—*i.e.*, as percentages of the quantity obtained by dividing the total work of the first set by 6—but the curves so obtained agree very closely in their general features with those of Fig. 6.

The curves make it very clear that in the case of this subject the increase at the beginning of each set was due to an effect on both number and height of the contractions, but that the decrease as the sets of ergograms were continued was entirely due to decrease in the number of the contractions, the curves for the height even remaining in some cases above those of the normal days, though not to an extent which would justify any decided conclusions as to the action of the caffeine in this respect.

This experiment points unmistakably to the action of caffeine as an accelerator of fatigue as it has been previously supposed to be by Féré, a mode of action of which there is no evidence in the experiments of the other subject.

There are some special features of this experiment which point to the effect being of a somewhat abnormal kind. Though the dose of 0·5 gramme has been taken by other workers without any very pronounced effects, it was certainly

an excessive dose for the subject in question, for his natural susceptibility to the influence of the drug had probably been much enhanced by more than two years' abstinence from all articles of diet containing caffeine. Further, the experiment was carried out in the extremely hot weather of September, 1906, and at the end of a prolonged period of very hard work. It is possible that the special mode of action of the drug may have been due to the combination of these conditions, and it is very unfortunate that, owing to the unavoidable limitation of the number of ergograms in each set, the earlier experiments were only able to give evidence of the initial increase, and we do not know whether with the smaller dose and more normal conditions of these experiments the same fall below the normal would have occurred. The last experiment shows conclusively that when taken in excess caffeine may act as an accelerator of fatigue, and the observations recorded in Appendix III. make it not unlikely that this mode of action is, at any rate in part, connected with the dulling of the sensations of fatigue. The peripheral mechanism is not restrained through the influence of the unpleasant sensations which normally take part in the inhibition of excessive activity.

The experiments of Mr. Webber and myself thus confirm, in general, the conclusion reached by all previous workers—that caffeine stimulates the capacity for muscular work; and it is clear that this increase is not due to the various psychical factors of interest, sensory stimulation, and suggestion which the experiments were especially designed to exclude. The greatest increase recorded in our experiments falls, however, far short of that described by some previous workers, such as Mosso, and it is probable that part of the effect described by these workers was due to the factors in question.

The chief interest of the new experiments lies in the clear demonstration of the very different way in which the same doses of the drug may act on different persons. In the case of one subject, the effect was so small that it is possible that the increase may have been due to chance variations from day

to day ; in the case of the other, the effect of the drug was so obvious as to place it beyond all doubt.

This great difference in the action of the drug quantitatively was accompanied by a still more important qualitative difference. In one subject the increase in the amount of work persisted throughout each set of ergograms ; in the case of the other the initial increase soon disappeared, to be replaced by a decided fall below the normal level.

With this general difference in the mode of action of the drug in the two subjects there was associated a difference in the effect on the two chief features of the ergogram—the number of contractions and their height.

In one (W.) the effect is predominantly on the latter, while in the other (R.) the number is chiefly affected ; but while in W. the effect throughout the sets is chiefly on the height, there is a slight initial effect on the number, and in the case of R. there is some indication of an increase in height, which persists throughout the sets in spite of the decrease in the total amount of work. The initial increase in the number of the contractions in the case of W. is suggestive of the existence, to a slight degree, of the mode of action which was so predominant in R., while the persistence in the increase of the height of R.'s contractions may be taken as evidence of the existence, in slight measure, of the prolonged effect which was so pronounced in W.

There is thus decided evidence of a double action of caffeine on the capacity for muscular work—one effect constant throughout a set of six ergograms, affecting chiefly the height of the contractions ; the other producing an initial increase followed by a fall, both dependent on the number of contractions. The former effect is one which may justly be said to diminish the effects of fatigue ; the latter is a transitory stimulation followed by so great a reaction that we are justified in speaking of the effect as one of acceleration of fatigue. In the subject W. there is evidence of both kinds of action, but the prolonged action predominates, the transitory increase being shown only in slight measure in the first ergo-

gram, and any reaction being altogether masked by the prolonged action. The last experiment of the subject R. seems to show that, in the conditions of that experiment, the action of caffeine as an accelerator of fatigue was so great as to mask almost entirely any prolonged action which may have been present, but that an indication of this latter mode of action is to be found in the increase of height, which persisted in spite of the falling off in number.

While the experiments show the existence of this double action with a high degree of probability, they tell us little about the nature of each kind of action. From this point of view, the most salient fact is that the prolonged action is predominantly on the height of the contractions, while the transitory action is chiefly on the number. Previous workers who have attended to the differential action of caffeine on height and number have found its action chiefly on the former, though a scrutiny of their figures shows that there has also been in many cases an effect on the number of contractions.

It has been supposed, especially by Kraepelin, that the action of caffeine in increasing height has mainly a peripheral seat, and if we adopt Kraepelin's hypothesis that peripheral action shows itself chiefly by affecting the height and central action by affecting the number, we shall find that the new facts are, at any rate, not inconsistent with it. We should expect a factor which produces an increase by central stimulation to be followed by a reaction; the effect of the central excitation would be to produce greater activity, the result of which would only be to exhaust the muscular mechanism more rapidly. The peripheral effect, on the other hand, may be due to some alteration in the supply of energy, whether the drug acts as an actual source of energy, or merely as a means of altering its economical use, which we might expect to show itself for prolonged periods.

That caffeine has a double action is not new. Observations on the isolated neuro-muscular mechanism have shown that caffeine has a peripheral action, and experiments on the capacity for mental work have shown that it has an effect on

central activity. The special interest of the new experiments is that the method of recording sets of ergograms separated by intervals of rest has permitted the demonstration of these two kinds of action in the performance of voluntary muscular work, and that the two modes of action may come into play so differently in different persons that an inspection of the results would make it difficult to believe that the same drug had been used in the two cases.

It is doubtful whether experiments on the capacity for voluntary muscular work alone can go far in the elucidation of this problem. Further results from this point of view must be hoped for chiefly from ergographic or dynamographic work in which the muscle is made to contract by electrical stimuli, and this means for the analysis of the complex action should go far to settle the question.

Influence of Caffeine on Mental Activity.

But little work has been done on the action of caffeine on the capacity for mental work. Kraepelin[1] tested the effect of tea on several mental operations, but his results give little indication how far this substance influenced the factor of fatigue.

In his later work with Hoch,[2] the influence of tea on mental fatigue was especially investigated, Dr. Hoch being the subject of the experiment, and the addition method being employed. Here, as in the work on muscular fatigue, the action of the two chief constituents of tea was tested separately. Caffeine was found to exert a favourable influence on the process of addition, while the influence of the essential oils of tea was rather less beneficial, but in each case the favourable influence was very slight. It must be remembered that in such experiments the estimation of the influence of any variation of conditions is rendered very difficult by the great increment in the amount of work which takes place from day to day under

[1] 'Ueber die Beeinflussung einfacher psychischer Vorgänge durch einige Arzneimittel,' Jena, 1892, S. 107.

[2] 'Psychologische Arbeiten,' 1896, Bd. i., S. 431.

the influence of practice, and, further, that the addition method is one in which the mental operations involved are of an extremely simple character, so that the work becomes almost reflex, and the part played by fatigue is relatively very slight.

The method employed by Hoch and Kraepelin gives no means of isolating the special factor of fatigue, and in choosing my own line of work it seemed desirable to make use of pauses during the work, so that the influence of the drug might be tested at different levels of fatigue, or, rather, at different stages of recovery from fatigue. In my first experiment in August, 1904, I used typewriting as the method of inducing fatigue. This cannot be regarded as a means of testing pure mental fatigue, for many motor elements are involved. The mental effort, however, in my case was considerable, for I was only beginning to use a typewriter, and I had not only to learn this new accomplishment, but at the same time to write as quickly as possible. On alternate days I took 0·3 gramme of citrate of caffeine ten minutes before beginning to work, and on the alternate days nothing, it being only during this experiment that I learnt how much one might be influenced by such a method of procedure.

In this experiment I had a distinct impression that I was doing better on the caffeine days, but the results showed little difference either in the absolute amount of work done or in the form of the curves.

The experiment, however, was rendered very unsatisfactory by the disturbance of my general condition, probably dependent—at any rate, in part—on the fact that I had only just given up the use of caffeine-containing substances as articles of diet. The great effects of practice, due to the fact that I was only just beginning to learn typewriting, also made it very difficult to estimate any effect which might have been due to the drug.

My next experiment with caffeine, in March-April, 1905, was one in which typewriting was done on twelve successive days, and was carried out under the most satisfactory con-

ditions away from all possible sources of disturbance. An hour's work was done on both morning and evening of each day, beginning at 9.45 a.m. and 5.45 p.m. On one group of days the hour's work was done continuously; on another group a rest of half an hour was taken at the end of half an hour's work, so that the programme was half an hour's work, half an hour's rest, and then again half an hour's work. On a third group of days an hour's rest was taken between the two half-hour periods of work. As the experiment lasted twelve days, four days' work was done under each set of conditions. During the first six days a dose was taken both morning and evening ten minutes before beginning to work; on some days the dose contained 0·3 gramme of citrate of caffeine, and on other days it was a mixture of gentian and citric acid. The disguise was complete, and so far as the taste was concerned, I had no idea at any time whether I was taking caffeine or not.

In each period of work the amount written in each five minutes was measured, this amount being expressed in centimetres. The quality of the work was also investigated, and the number and nature of the errors in each five minutes recorded. At the time of this experiment I had abstained from all articles of diet containing caffeine for six months.

At the end of the first six days it became obvious that something was affecting my sleep on some nights and not on others, and, as it seemed probable that this was the caffeine, I discontinued taking the dose in the evening, and took it only in the morning,[1] so that during the second six days the caffeine or control was only taken once a day.

The influence of the caffeine may be estimated in two ways—by comparing the total amount of work done on the normal days with that done on the days on which caffeine was taken, and by comparing the course of the work of the group of the caffeine days with that of the normal days. The first procedure is especially appropriate to bring out any effect on the general capacity for work, while the second procedure will

[1] See Appendix III.

show more the influence of the drug on the course of fatigue. Since it is especially with fatigue that we are concerned, I leave the results reached by the first procedure for another occasion, and confine my attention to the course of the work as shown in the curves of Fig. 7. These curves give the results for the work of the mornings only. In them the work of each five minutes averaged for the twelve days, six caffeine and six normal, is given as a percentage of the work of the first five minutes, and it will be seen that the caffeine curve rises at once above that for the normal days and remains above it throughout, the rise in the second half of the whole

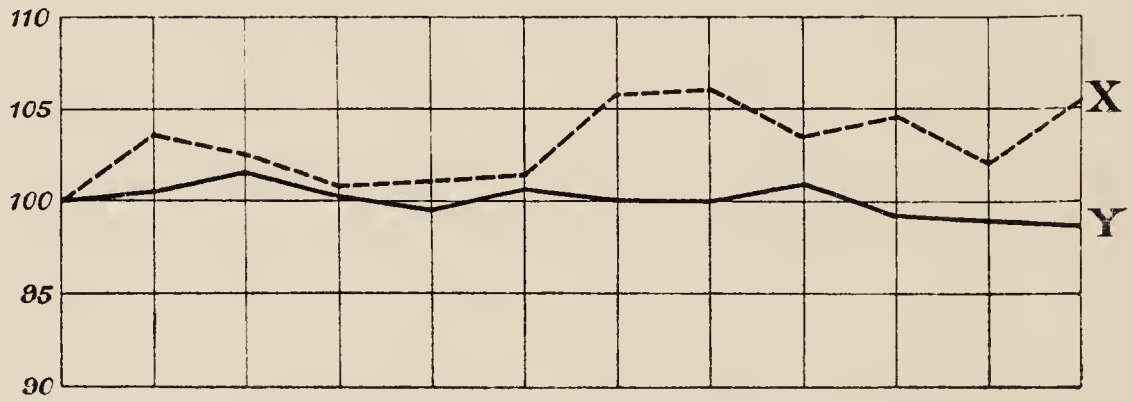

FIG. 7.—TYPEWRITING EXPERIMENT.
X, Caffeine, 0·3 gramme ; Y, control.

period of work being distinctly greater than in the first half-hour. It must be remembered that as the dose, whether of caffeine or control, was taken ten minutes before the beginning of the experiment of each day, the work of the first five minutes would itself have been to some extent influenced by the nature of the dose ; and if the dose had been taken after a certain amount of work had already been executed as a standard, it is probable that the effect of the caffeine would have come out still more strongly.[1] On the other hand, the caffeine days preceded the normal days throughout, and as the effects of practice gradually grow less from day to day, the caffeine curve would be raised to a greater extent by the effects of practice than the normal curves.

[1] This research was done before my work with the ergograph, and it was only while doing the latter that I learnt how essential it is to have a normal standard for each day before taking the dose.

In order to see how far this has been of influence, I have calculated the percentages, leaving out the first and last days of the experiment, which would leave ten days in which the normal days preceded the caffeine days. For the caffeine days the percentages run : 100, 102, 101, 99, 99, 100, 104, 104, 102, 102, 99, 102 ; while for the normal days they are : 100, 100, 101, 100, 99, 101, 100, 100, 101, 96, 98, 98. Thus there is little difference between the two curves in the first half-hour, but the superiority of the caffeine curve is almost as great in the second half-hour as when the whole twelve days are taken into account. Here any advantage accruing from the effects of practice would assist the normal days, and yet there is a distinct superiority of the caffeine days, and, though the increase is only slight, its occurrence in every five minutes' period of the second half-hour is in favour of its showing a real effect of the drug.

The number of mistakes of all kinds made in the type-writing was determined, and here it came out quite definitely that the drug was without influence. The total number of errors was not very large ; for the morning work it was 459 on the caffeine days, and 462 on the normal days. As might be expected, the number of mistakes was somewhat greater in the second half-hour periods, the respective number for the caffeine days being 216 and 243, and on the normal days 209 and 253.

It is interesting that, as has been found in the case of arithmetical work, the number of errors should be relatively so small, and should fail so completely to show any trace of a drug-effect.

The only other research on caffeine which I have to record is one carried out in conjunction with Mr. McDougall, using his method of measuring fatigue of attention by estimating the accuracy of aim when dots are made to pass rapidly through a slit. The work with caffeine was done every morning at eight o'clock. The experiment lasted for nine successive days, on three of which a dose of 0·3 gramme of citrate of caffeine was taken ten minutes before beginning to

work. On the other six mornings were taken doses of two control mixtures, which to both of us were quite indistinguishable from that containing the caffeine.

On each day we began by aiming at eight rows, each of 120 dots; then rested for half an hour, and repeated the eight rows of dots. On some days we did the eight rows continuously; on other days we allowed an interval between two rows of the same duration as that occupied in the passage of a row; and on the remaining mornings the interval between two rows was twice as long. The time taken by the passage of each row of dots was 26·5 seconds, so that on some mornings work was executed for about three minutes continuously, while on other mornings there was an interval of 26·5 seconds after a period of work of the same duration, and on other mornings the interval was 53 seconds.

The results may be estimated in several ways, and I give here the total number of times that the dots were hit on the three groups of days, those on which caffeine was taken, and the two groups of days on which the two control mixtures were taken. I will give Mr. McDougall's figures first. In the first period he hit 1,576 dots on the three caffeine days, 1,606 dots on one group of control days, and 1,646 dots on the three days on which the other control mixture was taken. In the second period, after resting for half an hour, there were 1,571 hits on the caffeine days, 1,424 and 1,486 respectively on the two groups of control days. In the first period the number of hits on the caffeine days comes out midway between those for the two groups of control days, while in the second period the caffeine days are decidedly superior to either group of control days. This superiority of the caffeine days is not due to any effect of practice, for the order of the days was varied, and the experiment was only begun after preliminary practice, so that the amounts do not show any definite increase as the result of practice during the nine days that the experiment lasted.

The experiment in my own case was carried out on the same days and on exactly the same lines as that of Mr.

McDougall, and it agrees with his in showing no indication of a caffeine-effect in the first period, but a definite increase in the second. In the first period there were 1,459 hits on the caffeine days, and 1,511 and 1,602 on the two groups of control days in the first period; and in the second period 1,460 on the caffeine days, and 1,339 and 1,421 on the control days. As with the other subject, there was no definite increase from day to day during the nine days, and the larger amount on the caffeine days is certainly not due to the effects of practice.

It was, of course, arranged that the days with different pauses between the rows should be equally distributed over the caffeine and control days: thus, one caffeine day was done with no pause, another with a pause of 26·5 seconds, and the other with a pause of 53 seconds. These pauses had a very decided effect on the number of hits,[1] but the data are too few to allow any opinion to be formed whether the effect of the caffeine was influenced by the presence or absence of a period of rest between the periods of work.

There was one feature of method in this experiment which was only employed on this occasion—viz., the use of two control mixtures. This expedient was adopted chiefly in order to assist the disguise of the caffeine (for which purpose later experience has shown it to be unnecessary), but it brought out very clearly the great variability of the results from day to day in this method of studying mental fatigue. If we had used only one control, we might have thought there was a very decided caffeine effect, or a complete absence of effect, according to which control had been omitted; and the fact that the difference between the results with the two inactive controls was so great makes it clear that no importance whatever can be attached to the differences found in the first period of work, while the superiority of the caffeine days to both sets of control days in the second period makes it almost certain that we have to do with a real effect, though the difference between the number of hits on the caffeine days and on one of the

[1] See *Brit. Journ. Psychol.*, 1905, vol. i., p. 442.

control days in my own experiment is not very great. These experiments are not very satisfactory, but it must be remembered that they were the first experiments with an entirely new method, and were designed chiefly as a test of the method. From this point of view the results are very hopeful, and there is little doubt that more prolonged experiments on the same lines would demonstrate clearly the nature of the action of caffeine on central activity.[1]

The experiments I have recorded by two different methods thus confirm the conclusion of Hoch and Kraepelin that caffeine has a stimulating action on the capacity for mental work, though the increase is not very great. There is thus clear evidence of the influence on central activity which I have supposed to take a part in the action of the drug on the capacity for muscular work. The increase of mental activity which followed the administration of caffeine in myself is slight compared with the effect recorded in the work with the ergograph, and yet the dose of the drug and general conditions of the experiment were much the same in my earlier ergograph experiments as in those on mental activity.

These observations on the capacity for muscular and mental work in the same person thus show a decidedly greater effect of caffeine on the former, and this may perhaps be regarded as confirmatory of the view that, in the case of muscular work, the central action of the drug is supplemented by a peripheral action, though there are, of course, other possible explanations of the difference.

In my typewriting experiments the work was carried on continuously for half-hour and hour periods, and there was thus abundant opportunity for the appearance of any such reaction as occurred in my last experiment with the ergograph ; but in this experiment the dose of the drug was considerably larger, and the state of health of the subject less satisfactory, so that the two experiments are not comparable. So far as it goes, the typewriting experiment tends to confirm the view

[1] For the results of further experiments, see W. McDougall, *op. cit.*, p. 441.

that the special nature of the action of caffeine in my last ergographic experiment was somewhat abnormal.

A point to which I may here refer shortly is concerned with the rate of action of the drug. In the last recorded experiment there was no evidence of the influence of the drug ten minutes after its ingestion, and in my typewriting experiment the decided rise in the curve only occurred during the second period of work, which varied on different days from 40 to 100 minutes after the drug had been taken. There is evidence in these experiments that caffeine acts very slowly, but that its action persists for a considerable time.[1]

With the ergograph the behaviour of the drug is different. In my own last experiment there was no evidence of the action of the drug from ten to twenty-five minutes after it was taken, though the effect had become most pronounced after fifty-five minutes. In my earlier experiments, on the other hand, and in both Mr. Webber's experiments, the effect was present ten minutes after its ingestion. There is no reason why the rate of absorption should have differed in the different cases, and the suggestion which occurs most naturally is that the central effect develops slowly, while the peripheral effect is able to show itself rapidly. I have pointed out reasons for believing that the very pronounced effect in my third ergographic experiment had a central seat, and if we accept the above suggestion, the discrepancy between the results of this experiment and both my earlier experiments and those of Mr. Webber is explained : in the former the effect was almost entirely central, while in the latter it was peripheral.

I acknowledge that we are here very much in the region of conjecture, but it is perhaps significant that several features of the action of caffeine on mental activity should thus fall into line with the view that the effect of caffeine on muscular activity has a twofold nature.

The general practical conclusions to be drawn from the experiments which I have recorded, and from those of previous

[1] For other evidence of the persistence of the central action, see Appendix III.

workers, is that caffeine increases the capacity for both muscular and mental work, this stimulating action persisting for a considerable time after the substance has been taken without there being any evidence, with moderate doses, of reaction leading to a diminished capacity for work, the substance thus really diminishing and not merely obscuring the effects of fatigue. The results of one experiment, however, point unmistakably to the conclusion that, when taken in excess, the stimulating action may be so transitory, and followed by so great a decrease, that it may legitimately be spoken of as an accelerator of fatigue; and it may perhaps be pointed out that the general conditions of this experiment were just those in which there is great danger that substances containing caffeine may be taken in excess. The experiment suggests strongly that caffeine is a dangerous remedy as a stimulant in cases of prolonged fatigue, or of that enhanced tendency to fatigue which is the characteristic feature of neurasthenia.

LECTURE III

ALCOHOL

Alcohol and muscular fatigue; historical; new experiments with ergograph; absence of effect with doses varying from 5 to 20 c.c. of pure alcohol; previous results due to defective control; inconstant increase with dose of 40 c.c.

The experimental work on the action of alcohol which has hitherto been recorded is far less satisfactory than that on caffeine, of which I gave an account in the last lecture. Though many workers have tested the effect of caffeine by giving it in one of the forms—tea, coffee, etc.—in which it is taken in everyday life, we found that we had some data[1] to enable us to distinguish how far the effects of these substances are due to their caffeine, and how far to other active principles they may contain. Alcohol, on the other hand, has been given in the most varied forms, and—except for those who have used pure ethyl alcohol—hardly any two workers have used the same means of administering the substance. Further, nothing has been done towards discovering what are the separate actions of the different constituents of the alcoholic beverages which have been used, as has been done in the case of tea and kola, and we have no evidence to tell us how far the effects which have been described are due to the alcohol or to other constituents.

The pungent flavour of alcohol is particularly adapted to produce effects on the capacity for work by its stimulating action as it is being taken into the mouth and swallowed, and this stimulating action is very much enhanced when the substance is taken in one of the forms in which it is habitually used. Further, very much of the work on alcohol has been

[1] Especially in the work of Hoch and Kraepelin, and of Mosso.

undertaken with an obvious bias, induced by enthusiasm either for temperance or for the virtues of alcohol, and owing to the very great influence of emotional factors, especially on the ergographic curve, a bias may be a grave source of error, even if the most earnest endeavours are made to overcome it. Yet, with all these obvious dangers and sources of error, no one has attempted to use in his experiments the control which would have removed the most serious of these dangers.

The first worker to use the ergograph for the investigation of the action of alcohol was W. P. Lombard.[1] He made only a few experiments, taking small doses in the form of claret. With voluntary contractions he found an increase in the amount of work, the effect showing itself in a few minutes, and lasting in one case for an hour and a half. With contractions produced by electrical stimulation, on the other hand, Lombard found the amount of work was diminished, and he concluded that the favourable effect of the alcohol was due to some central action.

Two years later Rossi[2] tested the action of alcohol in the form of rum on the work executed in fifteen ergograms, taken at intervals of ten minutes. With doses of 80 grammes, corresponding probably to about 30 grammes of absolute alcohol, he found an increase in the total amount of work; but this increase was chiefly due to the earlier ergograms, the later showing a decrease as compared with the work of days on which no alcohol had been taken. With smaller doses of 25 grammes of rum the favourable influence was more pronounced, and persisted for the whole of the two hours during which the experiment lasted.

The next work on the action of alcohol excited great interest, and may be regarded as the starting-point of a series of investigations designed either to support or overthrow it. This was the work of Frey, published in 1896,[3]

[1] *Journ. Physiol.*, 1892, vol. xiii., p. 49.

[2] *Rivista sper. di Freniatria*, 1894, vol. xx., p. 448.

[3] 'Ueber den Einfluss des Alkohols auf die Muskelermüdung. Mitth. aus Kliniken u. med. Instituten der Schweiz,' Reihe iv., Heft i. Basel u. Leipzig, 1896.

which had its origin in the accidental observation that a glass of beer had a great effect on a patient who was being tested with the ergograph to ascertain the degree of recovery of a paralysed limb.

Frey found that the action of alcohol on the fatigued muscle was different from that in the fresh condition. When alcohol was given ten minutes before beginning to work with the ergograph, the effect in most persons was to diminish the amount of work, the decrease being due chiefly to diminution in the height of the individual contractions. In the exceptional cases in which more work was done under the influence of alcohol, the effect was due to increase in the number of the contractions, the height still remaining below the normal. In spite of the actual decrease in the amount of work, it seemed to the subject that the work was being done more easily, and Frey records that this was so pronounced in his own case that he thought he must be using too light a weight.

If, on the other hand, the alcohol was given after a certain number of ergograms had been recorded, so that some fatigue had been induced, Frey found that alcohol had a beneficial effect, and that the increase in the amount of work might be considerable. From these observations he concluded that alcohol has a double action—an injurious action on the nervous system, which predominates when the muscle is unfatigued, and a beneficial action as a food for the muscle substance.

Frey's work is open to many serious objections. He gave his alcohol in all sorts of forms, and in the most varied, though in all cases small doses, and though he states that his conclusions are drawn from a large number of observations, he gives the reader no data for the exact study of the curves with and without alcohol. Further, his conclusions involve most improbable assumptions as to the value of alcohol as a food for muscle. He used very small doses, often not more than 5 grammes of alcohol after only three or four ergograms had been recorded. If we accept his con-

clusions, we should have to suppose that the work of the small group of muscles involved in work with the ergograph has so exhausted the nutritive substances contained in the blood that trifling doses of alcohol exert a decided beneficial action which much more than outweighs the injurious action on other parts of the neuro-muscular mechanism. Except in one of his experiments with sugar, Frey made no attempt to use control substances ; but he regards the play of suggestion or other psychical factors as out of the question, because he found exactly the same differential action of alcohol when the contractions were produced by electrical stimulation of the muscles. Here again Frey gives so few data that it is very difficult to estimate the value of his experiments ; but it may be noted that his result is directly opposed to that obtained by Lombard.

Some of Frey's ergograms are so prolonged that they show with certainty that accessory muscles were allowed to come into play, his ergograph being of the original Mosso pattern.

The work of Frey aroused much interest and controversy, and in the following year a paper was published by Destrée,[1] in which he confirmed the conclusion of Frey that alcohol stimulates the tired muscle, but differed from him in finding the same effect on the work of the unfatigued muscle. In both cases, however, according to Destrée, the stimulating action is fugitive, and is followed by a fall in the amount of work below that of the normal. He also describes one case of a physician who, after the administration of 10 grammes of alcohol, became entirely unable to lift a weight with which he had half an hour previously performed 8 kilogrammetres of work. Destrée used very small doses of alcohol in the form of beer or brandy, corresponding probably in most cases to not more than 5 grammes of absolute alcohol, and there was not only no attempt to use control-substances, but usually

[1] *Journ. méd. de Bruxelles*, 1897, Nos. 44 and 47. I have been unable to obtain a copy of this journal, and my knowledge of Destrée's work is derived from a translation in the *Medical Temperance Review*, 1899, vol. ii., pp. 54 and 76.

no real control experiments at all. He believed that the stimulating effects disappeared in about fifteen minutes ; and this result is so greatly in conflict with those of other workers as to make it almost certain that his results were largely due to accessory factors, and give no real indication of any true alcohol-effect.

In the same year was published a paper by Tavernari,[1] who found that 50 grammes of Marsala wine taken after a walk of thirty kilometres doubled the amount of work executed with the ergograph. The curves he gives leave, however, little doubt that the increase was largely due to the presence of accessory movements as the muscles originally in action became fatigued.

I now come to observations recorded by Kraepelin, and based on work by Glück, which have not yet been published in full.[2] This work differs from most of that previously recorded, in that we are given definite figures, both for the normal days on which no alcohol was taken and for what may be called the alcohol-days. Two series of observations, each of eight days, were made, the first with pauses of ten minutes, and the second with pauses of three minutes, between the ergograms. The drug was taken in the form of ethylic alcohol in doses of 40 grammes, the amount being thus much larger than in the experiments hitherto considered. In all cases two ergograms were recorded before the alcohol was taken, and then the work was continued for three-quarters of an hour. In the first series, with pauses of ten minutes, there was a marked initial increase, which disappeared to a large extent in the second ergogram ; but the work remained above the normal level during the whole duration of the experiment until the last curve, which showed a slight sinking below the level of the normal days. The whole work showed an increase of 13 per cent. above that of the normal days, which was entirely due to increase in the number of the contractions, the alcohol having no effect on their height.

[1] *Rivista sper. di Freniatria*, 1897, vol. xxiii., p. 89.
[2] *Münch. med. Wochenschrift*, 1899, Jg. xlvi., S. 1365.

In the second series, with pauses of only three minutes, so that fatigue played a much larger part, the effect was different. There was a large initial increase of 30 per cent., which disappeared in the second ergogram, from which point there was a diminution in the amount of work, so that at the end the total work was only half that of the normal days. This falling off in the latter part did little more than counteract the increase at the beginning, for the decrease in the total amount of the work of the whole period was only 5 per cent. This was due to a decrease in the heights of the contractions, the numbers showing on the whole a slight increase. In another series, in which sets of three curves were taken throughout the day at intervals of one or two hours, this diminution in the amount of work was found to continue for ten hours, the effect depending on a diminution in the height of the contractions.

In this year also Schumburg[1] published a few observations on the effect of alcohol, in which exactly the same method was used as in the work on caffeine considered in the last lecture. He claims that in uncomplicated ergographic work alcohol had a beneficial influence, but that in the presence of general fatigue produced by work with the ergostat, it had no influence. Only three alcohol experiments, however, were made—one with and the others without general fatigue, and with a dose of only 10 c c. In these experiments Schumburg compared the effect of alcohol with that of a mixture flavoured with dulcin, but there can have been here no question of a disguise.

In the same year appeared a dissertation by Heck[2] containing some critical considerations by Professor Fick, in which it is shown that the amount of alcohol taken by Frey was quite insufficient to produce his results if it were acting merely as a food-substance. The dissertation also contains a fragmentary record of experiments with a form of spring

[1] *Arch. f. Anat. u. Physiol.*, Physiol. Abth., Suppl. Bd., 1899, S. 289.

[2] 'Ueber den Einfluss des Alkohols auf die Muskelermüdung,' Inaug. Diss., Würzburg, 1899.

ergograph devised by Fick, in which no favourable effects of alcohol could be detected (the dose is not recorded).

In 1900 appeared the work of Scheffer,[1] who used Mosso's ergograph, but, as his tracings show, in a very different manner from that ordinarily employed. He raised a weight of 5 kilogrammes 150 times at a rhythm of one second, then, after five minutes' rest, again made 150 contractions, and after another pause of five minutes lifted a weight of 6 kilogrammes the same number of times. If Scheffer could do this, he must have been either a man of enormous muscular strength, far beyond anything encountered by any other worker, so that the weight of 5 and 6 kilogrammes was far below his maximal load, or he was using many more muscles than those ordinarily involved in working with Mosso's ergograph, and his results cannot be immediately compared with those of other workers. Ten grammes of absolute alcohol were taken immediately in one series, and fifteen minutes before the beginning of the work in another, and in each case the amount of work was increased. In a third series, in which the same dose was taken thirty minutes before beginning to work, the effect was unfavourable, a smaller amount of work being done with alcohol throughout.

One feature in Scheffer's paper is of interest from the point of view of individual differences. Scheffer is the only writer on the effect of alcohol who has given any indication of the method of action of the drug upon himself in ordinary life—an effect which is obviously of a depressing character. He notes that the depressing features—slackness, swimming in head, etc.—usually come on about twenty-five minutes after ingestion. Scheffer's results seem to show that in himself the small dose of 10 grammes is able to produce a temporary increase followed by a depression, corresponding in point of time to that of his subjective experiences. It must be noted, however, that he used no control, and in the absence of this precaution his conclusion must be received with caution.

[1] *Arch. f. exper. Pathol. u. Pharmakol.*, 1900, Bd. xliv., S. 24.

In 1900 there also appeared work by Féré,[1] who found that the act of keeping alcohol in the mouth while working had a greater effect on the ergographic record than when the same quantity was swallowed. Thus, it was found that if 20 c.c. of a mixture of equal parts of absolute alcohol and water were kept in the mouth while the record was being taken, the amount of work was nearly doubled, the effect being due to a great increase in the number of the contractions, which were more than trebled. Féré also tried the effect of putting the same quantity of alcohol into the stomach by a tube, and found a distinct decrease in the amount of work, which, as he remarks, may have been due to the act of passing the tube ; but it does not appear to have occurred to him to try the control experiment of putting some inactive substance into the stomach by means of the tube ; nor did the fact that sensory stimulation has so great an influence on the capacity for work lead him to adopt the measure of using control-substances in his work.

In 1901 appeared an account of work by Oseretzkowsky and Kraepelin[2] which had been done in 1894. Ergograms were taken at two minutes' interval, and after the seventh a dose of alcohol was taken, and the work was continued for an hour. The alcohol was only taken on four days, 15 grammes being taken twice, and 30 and 50 grammes on the other two days. On one day the dose of 15 grammes produced an increase, which continued to the end of the experiment ; on the other day there was a slight falling off as compared with the average of three normal days. The doses of 30 and 50 grammes produced very little effect. In this paper there are also recorded experiments by Moskiewicz with a dose of 30 grammes taken on three days, which showed a slight increase on the alcohol days, due entirely to increase in the number of contractions, the height showing a distinct diminution.

[1] *C. R. de la Soc. de Biologie*, 1900, p. 825. See also 'Travail et Plaisir,' Paris, 1904, p. .

[2] 'Psychologische, Arbeiten,' 306, 1901, Bd. iii., S. 620.

In 1903 Schnyder[1] published an interesting paper, in which he gives evidence that the effect of alcohol may be different according as it is taken soon after a meal or at a considerable interval. He used a simple form of Mosso's ergograph devised by Dubois. His first observations were made four hours after a meal. 6 to 12 ergograms being recorded at minute intervals. The alcohol was taken in the form of claret, and in such an amount that the dose of absolute alcohol would be about 15 grammes.

In one series the alcohol was taken fifteen minutes before beginning to work by two subjects, and in both cases there was an increase in the total amount of work, amounting to 10 per cent. in one case and 5 per cent. in the other—*i.e.*, the increase was not very great.

In a second series the effect of alcohol was compared with that of tropon, and the action of the former was found to be negligible, while the tropon produced a distinct increase, chiefly by affecting the number of the contractions.

In a second set of experiments Schnyder tried the effect of 30-gramme doses of alcohol taken during a meal, so as to show the effects of alcohol as taken in ordinary life. Here in both subjects there was a decrease in the total output of work, though not of any very large amount. In both subjects the effect of alcohol showed itself in diminution of the number of the contractions, while the height of the contractions was increased. Schnyder notes that the effect was so marked as to produce an obvious effect on the general form of the ergogram, those on alcohol days being tall and slender as compared with the normal curves.

According to this observer, then, the effect of alcohol varies with its relation to a meal, increasing the amount of work when taken in the fasting condition, and decreasing it when taken after or during a meal. He ascribes the difference to the action of alcohol as a food. He supposes that alcohol has a tendency to act injuriously on the nervous system in both cases, but that this injurious action is more than counter-

[1] *Arch. f. d. ges. Physiologie*, Bd. xciii., S. 451.

acted if there is a deficiency of nutritive materials in the blood.

In 1903, also, Frey[1] returned to the subject, with a critical study of the researches of those workers who had disagreed with his results. In his book he gives curves representing the results of some further experiments on the action of alcohol, confirming his previous conclusions so far as the action on fatigued muscle was concerned, both when the fatigue was produced by sets of six ergograms at intervals of a minute and when ergograms were repeated at the same rate till complete exhaustion was produced. Alcohol in the dose of 10 grammes was given at different times in the course of the ergographic record, and was found to produce a definite increase immediately after its ingestion, which persisted as long as the observations were continued, in one case for nearly two hours after the alcohol had been taken.

Frey also records further observations in which the effects of alcohol, sugar, coffee, and caffeine were compared with one another. Alcohol produced the greatest increase, sugar and coffee a slighter effect, and caffeine hardly any increase at all, although given in a dose almost certainly larger than that contained in the dose of coffee which had a much greater influence ; the order of potency of action thus corresponding with the order of the pleasantness and probable interest of the four substances. Frey thus himself provides evidence which suggests strongly that his results are due—at any rate, in great measure—to the effects of interest and sensory stimulation.

The next work on alcohol, in 1904, is that of Hellsten,[2] who used the ergograph already mentioned in the last lecture, by means of which work is done with many more muscles than with Mosso's instrument. It will be remembered that one feature of the work of Hellsten is the long time devoted to produce complete training before he began to use drugs, and his work has therefore been done on highly trained

[1] 'Alkohol u. Muskelermüdung,' Leipzig and Wien, 1903.
[2] *Skand. Arch. f. Physiol.*, 1904, Bd. xvi., S. 160.

muscle. He took his alcohol in the form of brandy, and in his first experiments took doses which contained 25 and 50 grammes of absolute alcohol either five or ten minutes before beginning to work, and found that the effect of the alcohol was so slight that the differences on different days might be due to chance variations. A much larger number of observations were made with a dose of 80 grammes, which Hellsten found to produce a distinctly injurious effect. In a series consisting of five normal and five alcohol days, on which the dose was taken thirty minutes before beginning to work, the average of the total amount of work on the alcohol-days was 5,111 kilogrammetres, and that of the normal days 5,967 kilogrammetres; and, further, the inferiority of the work done under the influence of alcohol comes out on every one of the days during which the experiment lasted.

In a further series, Hellsten tried the effect of the same dose of alcohol taken at different intervals—immediately, thirty minutes, an hour, or two hours—before beginning to work.

In all cases the alcohol diminished the amount of work, the diminution, when taken two hours before beginning to work, amounting to 11 per cent., while it was 17 per cent. when taken an hour before. These results refer to the total amount of work done during twenty ergograms, but when the alcohol was taken immediately or shortly before beginning to work there was an initial increase, which came to an end the more quickly the larger was the dose of alcohol.

The work under the influence of alcohol was characterized throughout by the fact that less work was done in each second, even when the total amount of work was greater. This means that the height of the contractions were diminished, so that Hellsten agrees with those other observers who have found that any favourable effect of alcohol shows itself by increasing the number rather than the height of the contractions. As regards the form of the curve, Hellsten found that under the influence of alcohol it approached a

straight line, and even in one case became concave, while in normal experiments the curve was, as usual, always convex.

The work of Hellsten is the most extensive which has hitherto been done on the action of alcohol, and at the same time it is the only work which can be said clearly to prove the injurious influence of alcohol on the capacity for muscular work. It must be remembered that he was using the very large dose of 80 grammes in the experiments which gave any decisive result—much larger than that used in any other work, and so large that disturbances of digestion were produced which made it necessary to discontinue the experiments. Nevertheless, in spite of this very large dose, the diminution in the amount of work was not very great, and cannot be compared with such a result as that of Destrée, in which a dose of 10 grammes was found in one person to abolish completely the power of lifting a weight which had been lifted readily in the normal condition.

The most recent work on alcohol is by Mlle. Joteyko,[1] who has studied the action of alcohol in several ways, though in each case her chief object has been to demonstrate the value of her method of mathematical analysis of the ergogram. She generally used small doses of 20 grammes of alcohol (it is left doubtful whether absolute alcohol or brandy), and found very great individual differences among the seven persons who were the subjects of experiment. Three were almost entirely resistant to the effect of alcohol, even when the dose was increased to 50 grammes, though two then showed a slight diminution in the amount of work. Two other persons showed a decided increase in the amount of work after doses of 20 to 30 grammes of alcohol, this increase being entirely in the number of contractions. The remaining two subjects showed a decided diminution—in one case even with 10 grammes of alcohol—and this action was so pronounced in one case that the weight could hardly be lifted at all after 20 grammes of

[1] 'Travaux du Laboratoire de Physiologie' (Instituts Solvay), Bruxelles, 1904, t. vi., p. 361.

alcohol had been taken. No evidence could be obtained in these cases of any initial phase of excitation.

On applying the method of mathematical analysis to a few characteristic curves, it was found that in most cases the parameter believed to indicate the activity of the central process was increased. Mlle. Joteyko had accepted the position held by Kraepelin and others that the exciting effect of alcohol is central, and therefore regarded this result as in favour of the validity of her mathematical method. The parameter believed to show the injurious influence of the products of activity was decreased in the majority of cases, the only exception being in the case of the subject on whom alcohol had a very pronounced beneficial effect, and Mlle. Joteyko explains this by the supposed action of alcohol as a food substance.

Mlle. Joteyko also investigated the effects of alcohol by another method, using the ergograms of Maggiora. With contractions executed by herself at the rate of one every ten seconds, there was no evidence of fatigue, even at the end of an hour. When the rhythm was altered to a contraction every eight seconds, fatigue supervened at the end of twenty-five minutes; but when this experiment was repeated after taking 20 grammes of alcohol, the curve remained at a constant level as long as the contractions were continued. With a rhythm of six seconds, it was found that fatigue normally showed itself in fifteen minutes, but after the same dose of alcohol there was no evidence of fatigue at the end of an hour. The contractions diminished slightly in extent at the end of the fifteen minutes, and then continued unchanged to the end of the experiment.

These ergograms with slow rate of contractions evidently provide a valuable modification of the ordinary method, and they seem to show that alcohol may prevent the occurrence of fatigue which would otherwise show itself; but it must be remembered that, in the absence of any control, the effect may have been due to purely psychical causes.

The commonly accepted explanation of the fact that the

curve does not fall off if the rhythm is sufficiently slow is that the time between two contractions is sufficiently long to allow removal of the poisonous products of activity, and Mlle. Joteyko therefore analysed these curves to see if there was any marked influence on the parameter supposed to indicate the effect of these products, and she found that, in accordance with her anticipation, it was enormously diminished.

Work on the influence of alcohol has also been done with the dynamometer. In 1892 De-Sarlo and Bernardini[1] found that doses of 70 grammes of rum produced a slight increase in muscular power, and in the same year Kraepelin,[2] with a dose of 30 grammes in one subject, and of 20 grammes in another, found a diminution. The drug was taken immediately before beginning to work, there being no normal on each day to act as a standard, and it is doubtful whether any great weight can be attached to the comparatively small differences which were found.

In 1899 De Boeck and Deladrier,[3] also using the dynamometer, found that rum in doses corresponding to 10 grammes of absolute alcohol diminished the contractions when the muscles were unfatigued. In the same year De Boeck and Gunzburg[4] tested the action of rum on a number of patients recovering from various forms of alcoholism, and found that, when the alcohol was given in the course of work with the dynamometer, varying effects were produced, a transient increase occurring in some persons, a decrease in others, while in others, again, no action was appreciable.

In 1900 Partridge[5] published observations with Salter's dynamometer, in which six sets, each of a hundred contractions, were made in an hour at a rate of one every 1·6 seconds.

[1] *Rivista sper. di Freniatria*, 1892, vol. xviii., p. 16.

[2] 'Ueber die Beeinflüssung einfacher psychischer Vorgänge durch einige Arzneimittel,' Jena, 1892, S. 91.

[3] *Journ. méd. de Bruxelles*, 1899, No. 4 (quoted by De Boeck and Gunzburg).

[4] *Bull. de la Soc. de Médecine Mentale*, 1899, p. 307.

[5] *Amer. Journ. of Psychology*, vol. xi., p. 371.

In one subject it was found that a dose of 20 grammes of absolute alcohol produced a decrease of power, while in another doses of 15 and 30 grammes had no decided effect on the total amount of work, though with the latter dose the course of the work showed that was an initial increase followed by a fall below the normal.

The results of this historical survey may be summed up as follows : Nearly all who have used the ergograph in their investigations have found that alcohol increases the capacity for work, either under certain conditions, or in certain persons, or for a certain time. Some, such as Féré, Destrée, and Kraepelin, believe that this increase is only temporary ; others, as Joteyko, that it only occurs in some persons. Of those who believe that the favourable effects of alcohol only make themselves felt under certain circumstances, Schnyder believes that the effect is only favourable when fasting ; Schumburg, as a result of very few experiments, believes that the opposite is true ; and Frey finds that alcohol only exerts its beneficial effect when the muscle is already fatigued ; and both Frey and Schnyder ascribe this beneficial influence of alcohol to its action as a food-substance.

Very different doses have been used by different workers. Some have found distinct effects produced by such small doses as 10 or even 5 c.c. of pure alcohol, or of beverages containing an equivalent amount. Others have obtained similar results with much larger doses, and one worker failed to obtain evidence of a definite effect till he had increased the dose to as much as 80 c.c. of pure alcohol.

When we turn to the details of the mode of action of alcohol on the ergographic curve, we find that the majority of those who consider this point find that the effect of alcohol is chiefly on the number of contractions ; but at least one worker—Schnyder—finds the exact opposite, alcohol, according to him, diminishing the number, while increasing the height of the contractions.

Some of the results may almost certainly be put aside as the result of imperfections in the ergograph employed. The

curves given by Tavernari and some of the earlier curves of Frey show that the increase due to alcohol was exactly of the kind which would be produced by accessory movements. They do not do more than indicate that the curve was continued longer under the influence of alcohol because other muscles were brought into play. A consideration of the curves given by many workers shows, however, that this can only be an exceptional cause of the increase in the amount of work.

A more frequent, and, indeed, universal, source of error is the complete absence of any adequate control. Heck found that alcohol had a beneficial result when combined with mental stimulation, which was absent without it; and Féré has shown that the effect of alcohol may be even more stimulating when it is taken into the mouth than when it is swallowed; but neither these nor other observers have compared the effects of two doses of similar taste and flavour, one containing alcohol and the other inactive substances. It seemed to me, in undertaking work with alcohol, that the first step was to test whether the effects described by Frey, Destrée, Féré, and others would appear if the factors of interest and sensory stimulation were carefully excluded.

The disguise is much more difficult than in the case of caffeine. With this substance we have seen that there is little difficulty in making two solutions, one containing the caffeine, and the other certain inactive substances which are wholly indistinguishable from one another. In my first work with alcohol on mental fatigue (see p. 98), a control solution was prepared for me by Dr. Dixon which contained capsicum, cardamoms, and a very small amount of chloroform, which was so much like a similar mixture with the addition of alcohol, that it was very difficult to distinguish the two from one another, when the dose of alcohol was small. The suspicion that one was alcohol was so indefinite that it could have had little influence, and the factors of interest and sensory stimulation were certainly present in equal measure with the two mixtures. Nevertheless, it

was probable that, with larger doses than I was using on this occasion, the alcohol would be recognized, and in the work with the ergograph I adopted the additional precaution of comparing the effects of two different doses of alcohol with the control in any one experiment. Dr. Dixon prepared three mixtures, one containing the substances already mentioned, one containing in addition a certain dose of alcohol, and the third containing double this dose. This use of two different doses of alcohol in any one experiment not only tended to enhance the disguise, but since it is to be expected that up to a certain point the effect of a drug will increase with the dose, the method should bring out indications whether in any given case an effect is really due to the drug, and the comparison between the effects of the two doses has often furnished useful evidence in the estimation of the value of an alteration in the amount of work. When two different doses are taken in this way during the course of an experiment, it may happen that the stronger of the two may be recognized, while the weaker fails to be distinguished from the control. If, then. in another experiment the former dose is combined with one still stronger, the now weaker dose may become wholly indistinguishable from the control, and this combined investigation of two doses may thus assist the disguise very materially.

Experiments of the Subject W.

As in the case of caffeine, Mr. Webber's experiments were more numerous and more satisfactory than my own, and I will begin with them.

Experiment 1.—The method employed was precisely the same as in the first caffeine experiment. Three sets, each of six ergograms, were recorded, with intervals between the sets of half an hour. The rhythm was two seconds, and the interval between the ergograms two minutes. The weight was 4·5 kilogrammes, and the drug or control mixture was taken ten minutes before the beginning of the second set of ergo-

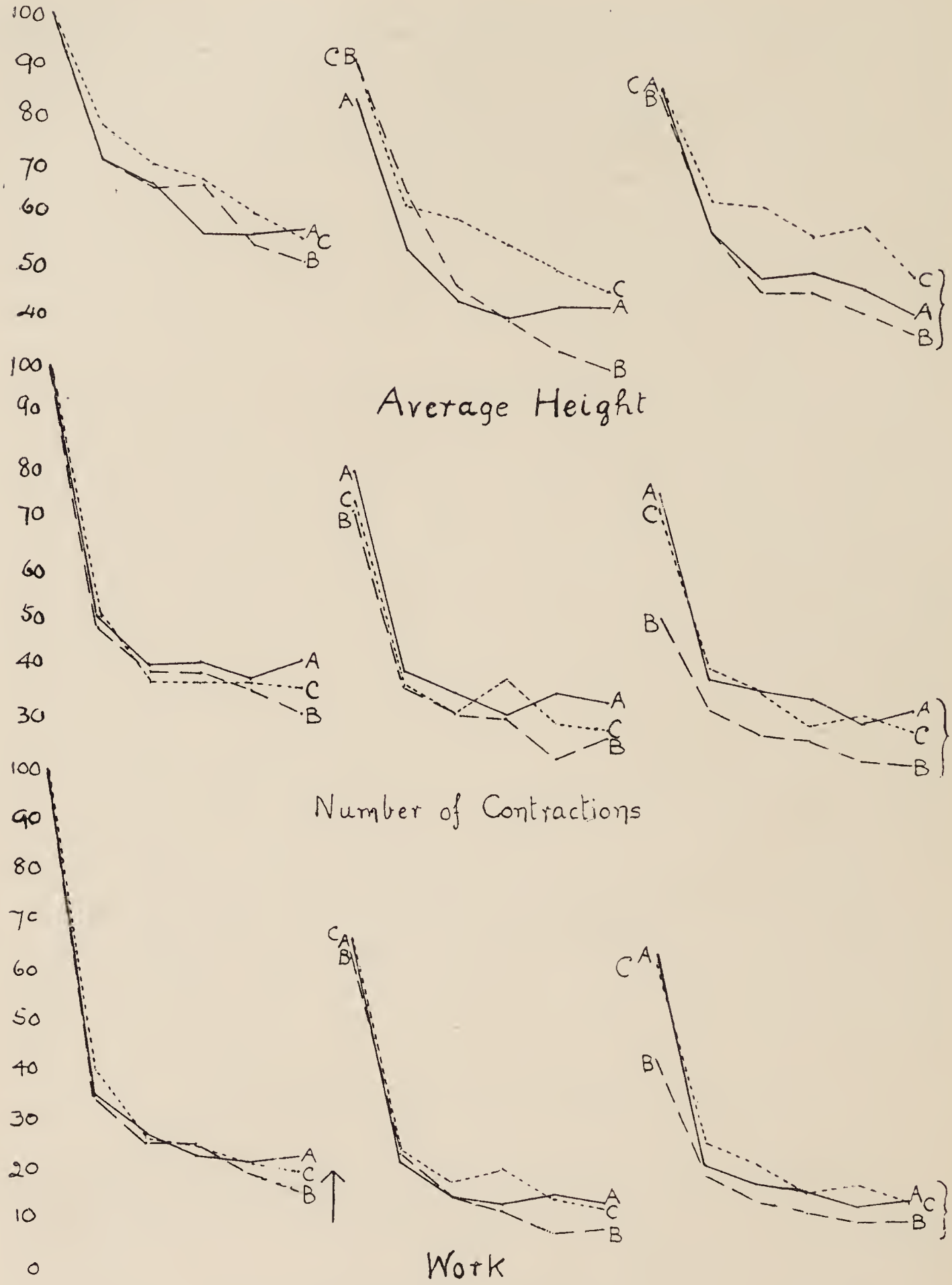

FIG. 8.—ALCOHOL EXPERIMENT W. 1.

A, Control mixture. B, Alcohol 5 c.c. C, Alcohol 10 c.c. Arrow shows when the dose was administered.

grams. The right and left hands were used alternately, and the doses were 5 and 10 c.c. of absolute alcohol. The experiment lasted for twelve days, so that 10 c.c. were taken on

four days, 5 c.c. on four days, and the control mixture of capsicum, etc., on the other four days, the three kinds of day being arranged in an order unknown to the subject.

The result is shown in Fig. 8,[1] in which the amount of work and the number and height of the contractions are shown in percentages of the first ergogram. The first sets were taken on all the twelve days before any dose had been taken, and A, B, and C days were therefore carried out under exactly the same conditions; and the very close correspondence of the three curves gives a most satisfactory tribute to the trustworthiness of the method, and serves to justify the device of expressing the results in terms of the first ergogram, the most notable difference in the last ergograms depending upon a condition which it is impossible to keep constant—viz., the amount of end-spurt.

The curves for the second set of ergograms, begun ten minutes after taking the dose, also run together very closely, showing that the alcohol had absolutely no effect either in increasing or decreasing the amount of work. The curves representing the heights of the contractions in this set show more deviation, that for the larger dose of alcohol falling off less than those for the other two days.

The third set, begun fifty-five minutes after the dose had been taken, shows at first sight a drug-effect; but it will be noticed that, of the two curves which begin with an increased amount of work, one represents the days on which the larger dose of alcohol was taken, while the other is that of the control days. It is very unlikely that a dose of 5 c.c. would produce a deleterious effect an hour after it was taken, while the larger dose of 10 c.c. had no effect, and the small amount of work performed on the 5 c.c. days may confidently be ascribed to adventitious circumstances of some kind. These curves thus bring out very decidedly the advantage of the method of combining two doses in one experiment.

In the curves representing height, that for the larger dose

[1] For the actual figures on which these and the following curves are based, see *Brit. Journ. Psychol.*, 1908, vol. ii., p. 261.

of alcohol again shows less tendency to fall, and this may possibly be significant, though it will be noticed that the curve was showing a distinct tendency to rise in the first set, which was recorded before any dose had been taken. On the whole, we may regard this experiment as giving an entirely negative result; and later experiments make it highly probable that such variations as occurred are due to disturbing factors of some kind. In this experiment one hand was used on six days and the other hand on the other six. The curves for the two hands taken separately were much the same, but, as might be expected, rather more irregular than those for the two hands taken together; and the study of these curves tends to confirm the impression that any differences between the different sets of days were due to chance variations.

Experiment 2.—In this the general method and conditions were as in the first experiment, except that the doses of 5 and 10 c.c. were taken between the first and second ergograms of the first set, the special object being to test the statement of Frey that alcohol produces a decrease in the amount of work if taken before any fatigue has been induced. In giving the dose after the first ergogram, there was a departure from Frey's procedure; but if this had not been done, there would have been no normal standard for the work of each day.

The intervals in this experiment were occupied with mental work in the form of multiplication (see p. 93).

In this and all succeeding experiments the subject took his own readings, the two minutes' interval between successive ergograms affording ample time for this and for any necessary adjustments of the ergograph. That the subject should take his own readings has some disadvantages; but it was not always possible for another person to be present to record them, and unless this could be done in all cases, it was thought best that it should be done in none. The whole business of reading the scale and making any necessary adjustments so soon settles down to a steady routine that the subject is not led to think about the relations of the

readings he is recording; and it is probable that the method of taking one's own readings is really less disturbing than one in which the subject has two minutes of complete leisure between each pair of ergograms for reflection on the nature of his performance. Further, there is the great advantage that the presence of another person in the experimental room, with all the possible sources of disturbance involved, can be dispensed with.

The special interest of the second experiment lies in the failure of the control. The larger dose of 10 c.c. was definitely recognized on each occasion, and the presence of alcohol was suspected in the case of the smaller dose. The results represented graphically in Fig. 9 show a definite increase on the alcohol days—greater on those with the larger dose—and this increase was apparent immediately after the dose was taken. It continued to the end of the first set, and was also distinctly present in the first ergogram of the second set, this curve falling slightly below that of the normal days in the remaining ergograms. The curves for number and height of the contractions show that the increase in the amount of work on the alcohol days was chiefly due to an effect on the former, though there was also a slight increase in the height in the first set on the two alcohol days, the curve for the smaller dose, however, here rising above that for the larger.

The action of alcohol in this experiment was of the same kind as that which has been described by most previous workers—viz., an immediate increase followed by a reaction shown in a fall below the normal; and it is suggestive that this kind of action should have shown itself in an experiment in which there was a failure of the control, so that the feature of interest was awakened.

It must be noticed that these two experiments give results exactly the opposite of those found by Frey. This worker obtained no effect when the alcohol was taken before any ergograms had been recorded, an increase only occurring when fatigue had been induced by the performance of a certain

amount of work. These directly opposed results, however, may safely be ascribed to different degrees in the amount of

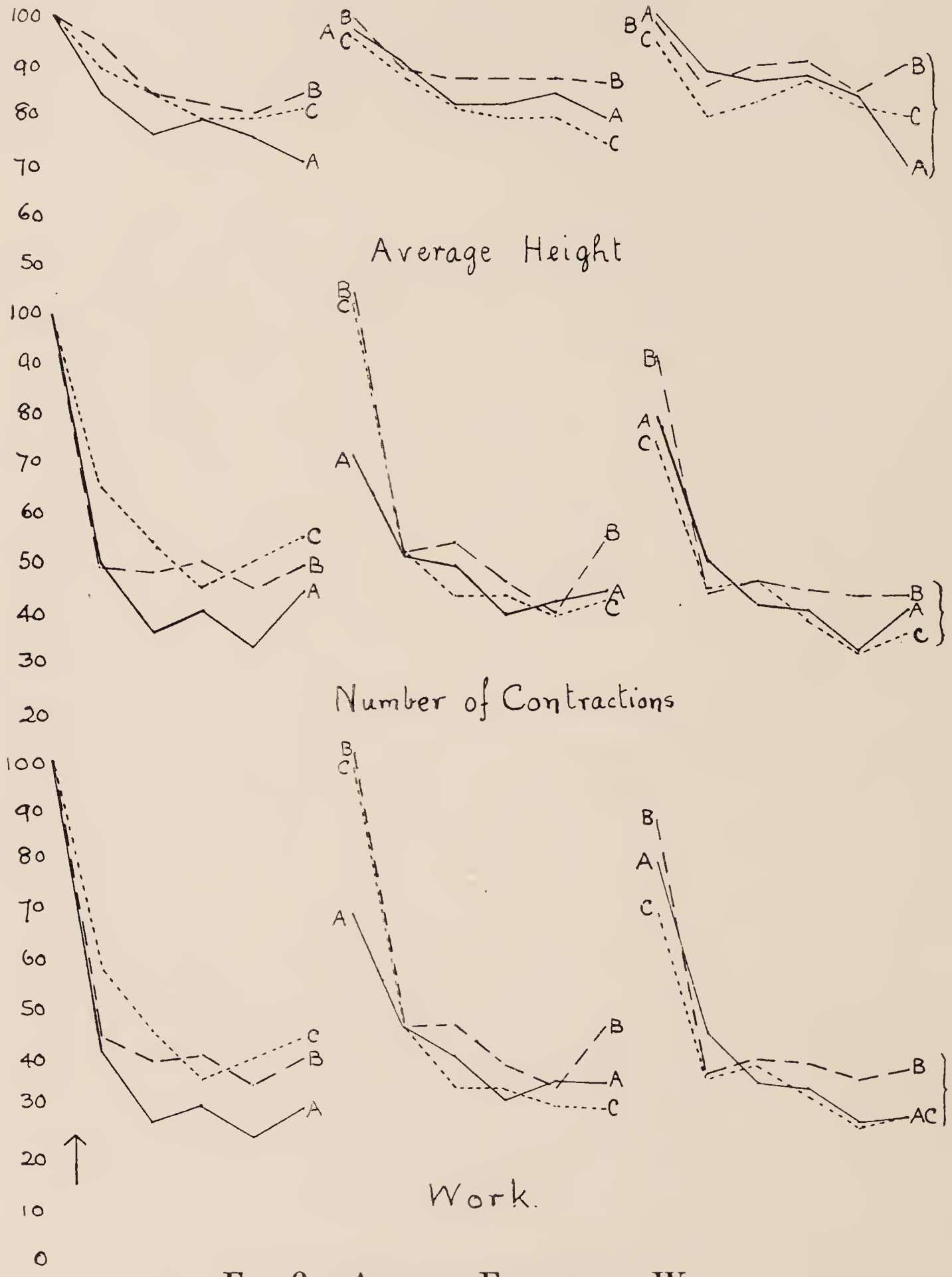

Fig. 9.—Alcohol Experiment W. II.
A, Control mixture. B, Alcohol 5 c.c. C, Alcohol 10 c.c.

interest in the different experiments, and they afford no indication of any true physiological effects of the alcohol.

Experiment 3.—The control having failed in the second experiment, it became necessary to modify the mixtures used for this purpose. The mixtures had so far contained capsicum, cardamoms, and chloroform only, to which Dr. Dixon now added some peppermint. The new control was completely successful, the disguise being so perfect that in the succeeding experiments the subject was wholly unaware, so far as taste was concerned, whether he had taken alcohol or the control mixture.

The third experiment was begun with the idea of testing the influence of doses of 10 and 20 c.c. of absolute alcohol by exactly the same methods as in the second experiment, except that the intervals on half the days were to be occupied with multiplication, while in the other half the place of the multiplication was to be taken by typewriting. At the end of five days the experiment was unavoidably interrupted, by which time only one day's work had been done with each dose. The smaller dose of 10 c.c. had given a completely negative result, while with the larger dose of 20 c.c. there had been an increase only noticeable in the first ergograms of the second and third sets. As there did not seem to be any evidence of a definite effect, we decided not to repeat this experiment, but to proceed directly to larger doses, especially as the dose of 20 c.c. was to be tried in the next experiment.

Experiment 4.—This lasted for twenty days, on six of which no dose of any kind was taken, on five the control mixture was used, while on the other days the doses of alcohol were either 20 or 40 c.c. of absolute alcohol. Each dose was taken between the first and second ergograms of the first set.

On each day four sets were recorded, each of six ergograms. The interval between the first and second and between the second and third sets was half an hour, but between the third and fourth sets it was increased to one hour. The first and second intervals were occupied with either multiplication or typewriting, the amount done in each five minutes being

recorded with the help of a five-minutes clock. This work was done for twenty-five minutes, leaving time at the beginning and end for the necessary adjustments of the ergograph.

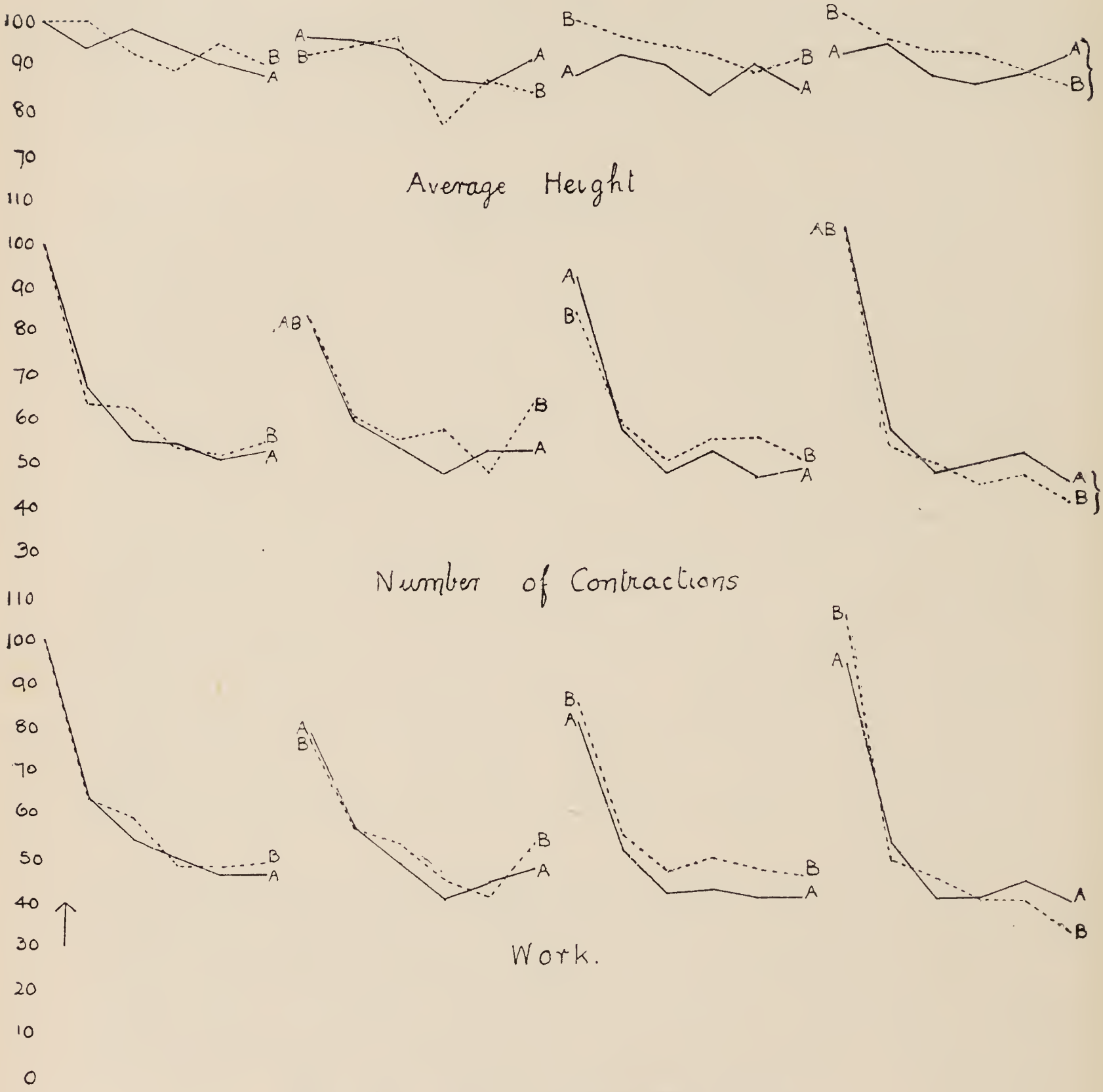

FIG. 10.—ALCOHOL EXPERIMENT W. IV.

Complete contractions. A, Control mixture. B, Alcohol 20 c.c.

The third interval of an hour was passed in gentle walking in the open air and in light reading, while a little food was also taken.

On some of the days the contractions were of the usual

kind; on the other days they were only allowed to reach two-thirds of their normal extent, as in my caffeine experiments (see p. 34 and Fig. 5).

In this experiment it became apparent that the alcohol was having a definite effect—at any rate, with the larger dose—and that the absence of the effects previously recorded was true only in the case of small doses. Since this absence of effect—due, I believe, to the use of proper control—is the subject to which I wish especially to call attention, I propose to consider the effects of the two doses used in this experiment separately, and I am the more willing to do this because the effect of the larger doses has not yet been established to my satisfaction, and is now the subject of further experiments by Mr. Webber.

In the following figures, therefore, are represented only the results with the dose of 20 c.c. The curve for the amount of work with the complete contractions given in Fig. 10 shows not the slightest trace of an immediate effect, and the two curves for the first set run together as well as if no drug had been taken. In the second set there is also no definite indication of an effect, which only appears in the third set, begun an hour and a half after the alcohol had been given. The fact that the alcohol curve in this set is consistently above that for the normal days suggests that we may possibly have to do here with a real drug-effect, though of only slight amount, which has wholly disappeared an hour later. The other curves show that this increase is due to an effect on both number and height of the contractions, perhaps chiefly on the former.

The results with the incomplete contractions shown in Fig. 11 seem to show an immediate depressing effect of the alcohol, but not of any great amount. In the second set this is replaced by an increase on the alcohol days, which becomes still more definite in the third set, to disappear in the last. This correspondence with the complete contractions in showing a definite increase in the third set is almost certainly significant, and seems to point to a stimulating action of the

alcohol asserting itself most definitely about an hour and a half after its administration. The increase is, however, very slight as compared with that recorded by Frey and others.

This fourth experiment thus confirms the first and third

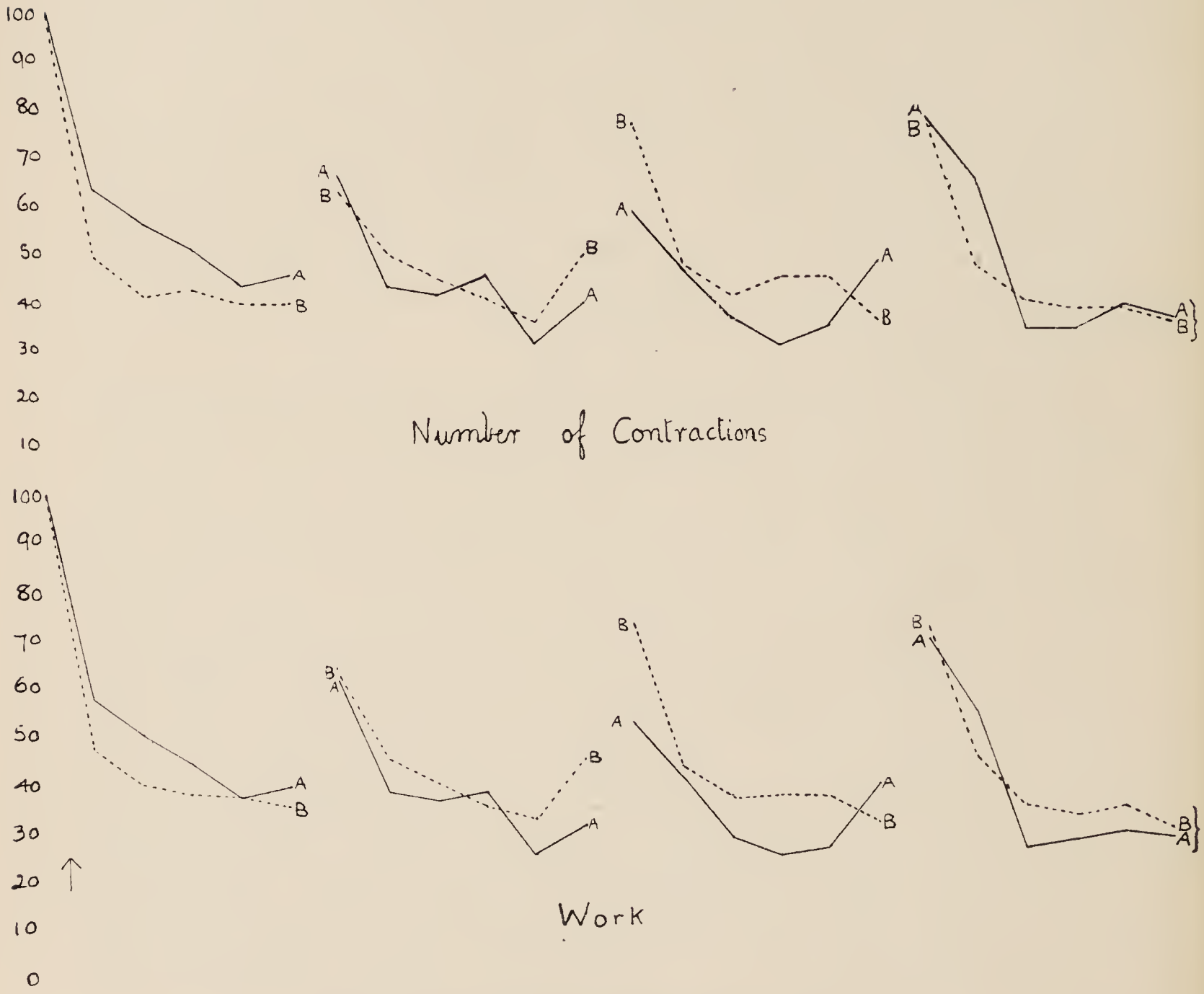

FIG. 11.—ALCOHOL EXPERIMENT W. IV.

Incomplete contractions. A, Control mixture. B, Alcohol 20 c.c.

in showing no trace of an immediate stimulating action when there is an adequate control, and any increase which is found is considerably delayed, being most pronounced about an hour and a half after the alcohol has been taken. The only definite increase thus occurs at a time when the effect described by most previous workers has disappeared, or a period

beyond that to which they have followed the effects of the drug.

A word must be said here on the validity of the procedure of expressing the results in their relation to the first ergogram. In the first alcohol experiment, and in the experiments with caffeine recorded in the last lecture, the dose of drug or control was not taken till after the first set had been completed, so that we are able to express the course of the work in terms of the whole of the first set as well as in terms of the first ergogram, and the correspondence of the two ways of expressing the results in those cases can leave little doubt about the genuineness of the results.

In the later alcohol experiments of W. the dose was taken immediately after the first ergogram, so that in this case we have only one ergogram to act as a standard. As a general rule, however, the course of the ergograms of the first set on the normal days is so constant, and the later ergograms stand in so definite a relation to the first, that one can have little doubt about the validity of our procedure. Still, in such a case there must always be the possibility that the first ergogram may be exceptional in some way, and in later experiments with other subjects the drug or control has not been given till a whole set has been recorded to act as a standard.

The Experiments of the Subject R.

My own experiments were much less satisfactory than those of W., owing to the muscular pain produced when sets of six, or even of three or four, ergograms were recorded. My first experiment was planned on exactly the same lines as the first experiment of W., with doses of 5 and 10 c.c. of alcohol, taken ten minutes before the beginning of the second set. This experiment could only be continued for five days, the results of which, though irregular, gave no indication of an alcohol-effect.

Experiment 2.—It was not possible to do any further satisfactory work till several months later, when, after pro-

longed training, a second experiment with incomplete contractions, lasting for six days, was carried out with doses of 10 and 20 c.c., taken one minute before beginning the second set. Five sets were recorded, each of four instead of six ergograms, as usual. As in our other experiments, the two earlier intervals were half an hour, and those between the later sets an hour, and all were passed in some light occupation or in the open air, the corresponding intervals on different days being always occupied in the same manner.

The figures for the individual ergograms in this experiment were very irregular, showing that the amount of practice was still insufficient, and this was also shown by the pain which the contractions still often produced. The first set was done before any dose had been taken, and the total amount of work done in this set was almost the same on normal and alcohol days. There was also no appreciable difference in the second set, begun a minute after taking the dose, there being thus no trace of an immediate effect. The third set showed an increase on the alcohol days, greater on the days on which the larger dose was taken, and therefore possibly significant of a real effect. This increase had disappeared in the following set, recorded an hour later, but there was no evidence of any reaction. The only evidence of an effect was, therefore, in the third set, begun three-quarters of an hour after the alcohol had been taken, but it is doubtful whether this increase was due to anything more than the irregularity caused by the imperfect condition of training.[1]

Experiment 3.—This lasted for six days, five sets, each of six ergograms, being recorded on each day with the right hand and with complete contractions. The doses of alcohol were 20 and 40 c.c., and they or the control were taken one minute before beginning the second set of ergograms. Even with the larger number of ergograms in each set, and though the contractions were complete, there was less pain than in

[1] For the full record of the results of this experiment, see *Brit. Journ. Psychol.*, 1908, vol. ii., p. 275.

the second experiment, and the form of the curves showing the course of the individual ergograms (see Fig. 12) is far more regular than in that experiment, though still far from attaining the regularity of the fully trained condition. As in the case of W., the results with the larger dose will be left till

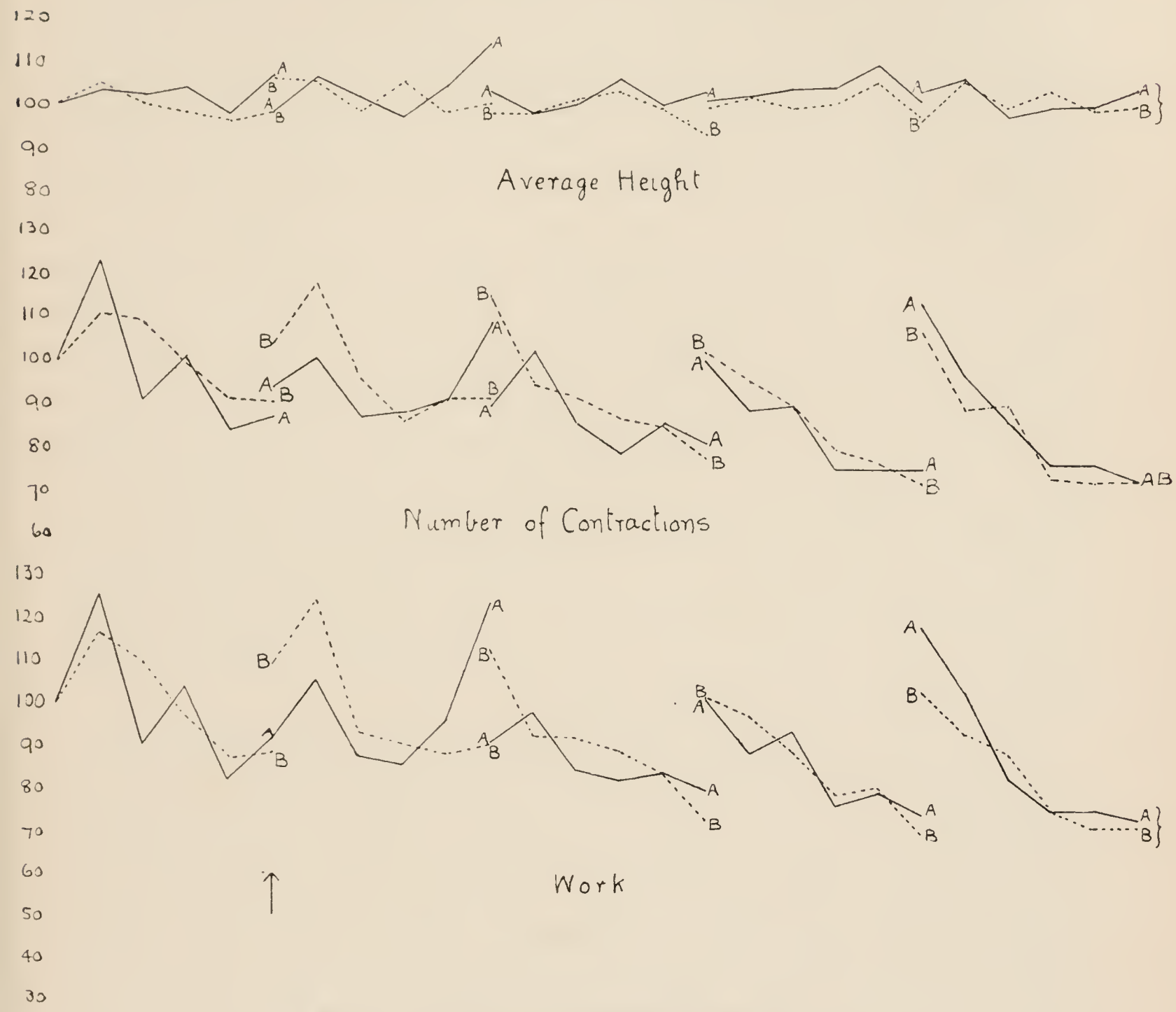

FIG. 12.—ALCOHOL EXPERIMENT R. III.

A, Control mixture. B, Alcohol 20 c.c.

later, and the curves for the control days and those on which 20 c.c. were taken are given in Fig. 12.

The curves show what may be an alcohol-effect in the second set begun almost directly after taking the dose, but the very abnormal form of the curve for the control days shows that much weight cannot be laid on the record of this

set. The first part of the control curve of the third set is also abnormal, probably owing to the existence of some pain, and it is only the first ergogram of this set in which there is any decided difference between the alcohol and control days, while in the fourth set the two curves run very closely together.

This experiment, then, differs from the preceding in giving a possible indication of an immediate effect; but, on the other hand, there is no trace of the increase after an hour and a half which occurred in the case of W., and the nature of the early increase gives one no confidence in its dependence on the action of the alcohol.

As in this experiment the dose was not taken till the first set of ergograms was concluded, it is possible to use the average ergogram of this set as a standard by means of which to express the course of the individual ergograms. Curves were, therefore, constructed resembling those of Fig. 12, except that each ergogram was expressed, not as a percentage of the first ergogram, but as a percentage of the average of the whole of the first set—*i.e.*, an average obtained by dividing the total work of this set by six. The curves so constructed, however, were found to agree very closely in their general features with those already given.

The chief result of the foregoing experiments is the failure to confirm the conclusion of nearly all previous workers that small doses of alcohol—from 5 to 20 c.c.—have an immediate stimulating or depressing action on the capacity for muscular work as tested by the ergograph. The experiments have differed from all previously recorded in the use of control substances, by means of which the days on which alcohol was taken were rendered indistinguishable from the normal days, and in the only case in which there was a definite immediate effect there had been failure of the control. The natural conclusion is that the results of previous workers have been due, not to the physiological effects of the alcohol, but to the presence of certain factors, and especially interest and sensory stimulation, the influence of which can only be excluded by the use of a control.

Before, however, accepting this conclusion, it is necessary to inquire whether there have been any other differences between our experiments and those of previous workers which might explain the divergent results.

One such difference is a consequence of the use of a control. The mixtures in which the alcohol was taken for purposes of disguise were decidedly unpleasant, and the possibility arises that this may have neutralized an effect which the alcohol might otherwise have produced. The control mixture containing no alcohol, however, was equally unpleasant, and as the unpleasantness was the same on both alcohol and control days, any alcohol-effect which existed ought to have become evident. Further, in later experiments carried out by Mr. Webber, a different control, decidedly pleasant to the taste, has been used, and in these experiments also there has been no evidence of an alcohol-effect.

Another possibility must be borne in mind. One of the most definite results of previous work on the action of alcohol has been to show the presence of great individual differences in the susceptibility to the action of the drug,[1] and though it is possible that these differences have been largely due to the part played by the psychical factors which it has been the especial object of the new experiments to exclude, there can be little doubt of the existence of true individual differences to the physiological action of the drug. It is possible that the two subjects whose work has been recorded in this lecture are especially resistant to the action of alcohol. The observations recorded in Appendix IV., however, show that W. is certainly not an example of insusceptibility; and I have no doubt that I have rather more than the average susceptibility to its general effects.

A further piece of evidence that the negative results have been due to the use of an adequate control is derived from a short experiment on the subject W. with doses of whisky containing 10 and 20 c.c. of absolute alcohol. These observations were made by giving the whisky without any attempt

[1] See p. 62.

at disguise, and it was found that both doses produced a very decided increase in the amount of work as compared with a normal day. The most noteworthy fact was that this increase was immediate, exactly as in most previously recorded work. It is, of course, open to anyone to say that the increase in this case was due to some component of the whisky other than ethylic alcohol, but the immediacy of its action can leave little doubt that we had to do mainly with the action of interest and sensory stimulation. If so, we have the clearest evidence that the cause of the negative results with pure alcohol in the case of the subject W. was not individual insusceptibility, but the means which were taken to exclude the psychical factors which have been allowed to influence all previous work.

There can be little doubt that the absence or slightness of the effects with small doses of alcohol which we have found are due to the use of control-substances, and that the results of most of those who have found the capacity for muscular work increased under the influence of such doses as 5 and 10 c.c. have been due, not to the physiological action of the substance, but to the interest aroused by taking the alcohol and the sensory stimulation involved in swallowing it, while those who have found a diminution in the amount of work must be open to the charge of having been influenced by suggestion.

Effect of Larger Doses.

The results so far dealt with have been derived from experiments with small doses, varying from 5 to 20 c.c. of pure alcohol. My special object in experimenting with these small doses was to test the correctness of the previous work of Frey, Destrée, Schumburg, Scheffer, Schnyder, and others, who had obtained what seemed to be evidence that these small doses had a definite effect, and I think the results so far recorded in this lecture can leave little doubt that the results hitherto published have portrayed, not the true physiological effects of alcohol, but merely the effects of certain accessory factors,

which these workers allowed to complicate their experiments. I have investigated with the ergograph the effects of a larger dose of 40 c.c., but I propose to deal with this portion of my work very briefly, partly because the results are indecisive, but still more because the effects of doses larger than 20 c.c. are now being submitted to further investigation by Mr. Webber —an investigation which, I hope, will enable us to speak as decisively about the effects of these larger doses as has been possible in the case of those which I have so far recorded.

The first observations with the dose of 40 c.c. were made concurrently with those already recorded. In the case of the subject W. there was a very pronounced increase with the complete, and a smaller increase with the incomplete, contractions. On examining the work of the individual days, however, there was found to be great irregularity, the increase being very decided on some days, and hardly present at all on others. The interesting feature of the increase, however, was the time at which it occurred. There was in each case no trace of the immediate effect, which has been so pronounced a feature of the results of previous workers. In the case of the complete contractions, not only was there no immediate effect, but the increase was hardly appreciable in the second set, begun three-quarters of an hour after the alcohol had been taken, and the effect was most pronounced in the third set, begun three-quarters of an hour later. In the case of the incomplete contractions, the effect was only slightly present in the second set, and as in the case of the complete contractions the increase was most decided in the third set, begun an hour and a half after the alcohol had been taken. This experiment was prolonged for over three hours, and the increase on the alcohol days was distinctly present in the final set; there was no trace of any decrease following the increase which other workers have found, although the experiment was continued much longer than in any previous research. Certain observations made by the subject of the experiments must, however, be taken into account in estimating the value of the results. So far as taste was concerned, the control used in this experiment

was almost completely successful, the nature of the different doses being rarely suspected ; but the subject was soon able to recognize the days on which the larger dose of alcohol had been taken by means of giddiness and other symptoms.[1] He therefore rapidly became aware that the larger doses, which were the special object of this experiment, were producing an effect—an observation which naturally aroused his interest, especially as it came after prolonged series of experiments in which the alcohol had usually had no definite effect. Further, as soon as the increase in the amount of work was decided, this was detected by the subject, and probably aroused his interest still further, and this fresh interest probably had some effect in accentuating the increase which was already showing itself. That this awakening of interest was the sole, or even the chief, cause of the increase I do not believe; but, in view of the negative results of later experiments —to be recorded shortly—the possibility of the explanation I have suggested should be borne in mind, and I have little doubt that any direct effect of the alcohol was supplemented by the factor of interest arising in the way I have supposed.

One interesting possibility was suggested by this experiment—viz., that the subject was, in spite of his lifelong abstinence, extremely resistant to the physiological effects of alcohol, and was exhibiting with this large dose of 40 c.c. the same effect which had been found by other workers with smaller doses. As I have already pointed out, however, the subject was probably rather more susceptible to the action of alcohol than the average; and, further, the effect was, of an absolutely different kind from that recorded in previous researches, for, instead of being immediate, it did not show itself in one case till an hour and a half after the substance had been taken, a period longer than the whole duration of the experiments of most other workers. Thus, in the work of Kraepelin's pupils, Glück and Oseretzkowsky, with doses of 40 c.c., the ergographic work was only continued on each day for about an hour after the alcohol had been

[1] See Appendix IV.

taken, a time at which the effects with the complete contractions in the case of W. had not yet shown themselves—*i.e.*, the effects described by these workers had run their course before those just described had even begun.

At its conclusion this experiment was taken to indicate a real alcohol-effect, which—at any rate, in the case of the complete contractions—persisted to the end of the experiment —*i.e.*, for over three hours. The special object of the next experiment was to ascertain whether this increase was followed by any reaction in the way of a decrease, and an experiment was arranged with the same doses (20 and 40 c.c.) as in the last experiment, but in which nine sets of ergograms were recorded, the first two intervals being of half an hour's duration, while the remaining intervals lasted for an hour, so that the total duration of the experiment of each day was between nine and ten hours. The experiment was continued for fifteen days, and its results were almost wholly negative. There was a good deal of irregularity, but the averages of the different groups of days showed little to which any weight could be attached. With the complete contractions the curves for the control days, and for those on which 40 c.c. of alcohol were taken, ran together very closely, while the days on which only 20 c.c. were taken showed a diminished amount of work. With the incomplete contractions, both alcohol days showed a distinct falling off as compared with the control days. So far as there was any difference between the alcohol and the control days, it went to show an injurious effect on the capacity for work, even from the beginning.

The experiment was in several respects less satisfactory than the earlier experiment with the same dose. The latter was carried out in May, when the subject was in good health and vigour, while the later experiment was in July, during the very hot weather of the summer of 1906. The subject felt the heat very much, and was distinctly below his normal level of health. Further, the whole experiment, continued for over nine hours every day, was very arduous and wearisome, and certainly could not have tended to improve the vigour

lowered by the external circumstances. It is probable that this lowered state of health made the general condition more variable from day to day, and the possibility cannot be excluded that the differences between the alcohol and control days are anything more than an expression of these variations. Another condition of the experiment which made the records of the subject more variable was the fact that the weight was not maximal. Several months had elapsed since he had begun to work with the ergograph, and in consequence his muscular power had increased considerably—so much so that, in the experiment under consideration, the weight had been increased to 5 kilogrammes, in order to keep within the limits of the scale on the wall of the laboratory. The more gradual fall of the curve for each set, however, as compared with that of the early experiments, makes it obvious that even this large weight gave the subject a task relatively smaller than before; the curves show that the subject was working with a submaximal weight instead of with a truly maximal weight, as in his earlier experiments. The results of this experiment suggest that the most favourable condition for bringing out a drug-effect is the use of a fully maximal weight, and that even if the weight is only slightly sub-maximal, the variations from day to day may be so great that they may mask any slight drug-effect.

I also carried out an experiment to test the effect of a dose of 40 c.c., the record forming part of the experiment already described with the dose of 20 c.c. In my case the effect of the larger dose was very slight, but in the direction of a decrease in the amount of work under the influence of alcohol. Here the dose was taken one minute before the beginning of the second set of ergograms, and the work of the first set on the days on which this dose was taken showed a distinct tendency to fall before the drug was taken. It is thus possible that the decrease on these days was nothing more than a continuation of this fall, and did not indicate a true drug-effect.

It will thus be seen that the results with the dose of 40 c.c. are variable. The experiments were open to reproach

from several points of view, and it will be best to suspend judgment till the results of further work, now in progress, are available. It is possible to say, however, that sometimes a dose of 40 c.c. of pure alcohol may produce a decided increase in the amount of work executed with the ergograph, but that at other times this increase may be wholly absent, and may possibly be replaced by a decrease.

In one point the results with the larger dose of alcohol agree with that of nearly all previous writers. Wherever alcohol produces any effect it is on the number of the contractions, and there is little indication that the height is at all affected by the drug. Many previous workers have found that the increase in the number of the contractions is accompanied by a decrease in the height, but this was certainly not the case in the experiments just described.

The effect of interest and mental excitement is chiefly, if not entirely, on the number rather than on the height of the contractions, and if the effect I have described with the dose of 40 c.c. is due to the physiological effect of the alcohol, this special action on number, rather than on height, might perhaps be held to point to a central action of the drug.

It will have been noticed that not only my own work, but also all the researches of other workers, have been devoted to the endeavour to ascertain the immediate effects of a dose of alcohol, and that I have said nothing of its more prolonged effects, as tested by comparing periods during which alcohol is taken regularly with periods of abstinence. The reason for this is that these prolonged effects have not yet been investigated by laboratory methods in the case of muscular work, though, as we shall see, an attempt has been made in this direction in the case of mental work.

Further, I have made little reference to the action of alcohol in general fatigue. My own work has been carried out in such a way as to exclude general fatigue as much as possible and to study muscular fatigue in its pure state, and this has also been the object of most other researches, Schum-

burg and Tavernari being the only workers who have attacked the problem of general fatigue directly, though this must have played a large part in the work of Hellsten.

The only cases in which the prolonged action of alcohol in general fatigue has been tested are to be found in the observations which have been made on large masses of men in campaigns, etc., and here the results point strongly to the conclusion that alcohol is prejudicial to the capacity for work and in no way helps to diminish the effects of fatigue.

The capacity for work, which is tested in any such mass observations, is of a very complicated nature. Any effect which alcohol may have on the capacity to hold out during a prolonged march, for example, is obviously very complex. In such a feat every organ of the body is involved, and far more is being tested than mere muscular fatigue, which is all that has been investigated in most of the researches to which I have referred in this lecture.

All that I and most others have attempted to do is to study the immediate effect of alcohol on one of the constituents of the complex—viz., pure muscular fatigue—and it must be the task of future laboratory research to determine which elements of the complex exert the injurious influence which the mass observations seem to demonstrate.

LECTURE IV

INFLUENCE OF ALCOHOL ON MENTAL FATIGUE

Historical; new experiments with multiplication, typewriting, and by McDougall's method; slightness of effects—Mode of action of alcohol in fatigue; comparison of effects on muscular activity of alcohol and mental fatigue; removal of controlling influence.

I WILL deal with the history of work on the action of alcohol on mental fatigue briefly. Nearly the whole of these researches come from the school of Kraepelin, and do not show the same contradictions as those with which we have met in the case of the action of this substance on muscular fatigue; but they have dealt rather with the action on the general capacity for work than with the factor of fatigue, and most of the researches have not been devised in such a way as to bring out any action on this special feature of mental activity.

In his book on the action of drugs on mental processes Kraepelin[1] deals with the action of alcohol on various forms of mental activity, but with little reference to fatigue, and I can pass on to the researches published in his 'Psychologische Arbeiten.' Of these, the one which stands in the closest relation to the other researches I have been considering in these lectures is that by Aschaffenburg,[2] on the influence of alcohol on four compositors.

The special feature of this work is that the four men were carrying out their usual occupation, and, as far as possible, in the usual way. All were in the habit of taking alcohol—one

[1] 'Ueber die Beeinflüssung einfacher psychischer Vorgänge durch einige Arzneimittel,' 1892, S. 41.

[2] 'Psychologische Arbeiten,' 1896, Bd. i., S. 608.

in somewhat excessive amount—and if there was any bias in this experiment, it was probably in favour of alcohol. The experiment lasted for four days, on two of which each man took 200 grammes of a Greek wine, containing 18 per cent. of absolute alcohol. The duration of the experiment of each day was an hour and a quarter, which was long enough to bring out a definite fatigue effect.

The results in the form in which they are given by Aschaffenburg show that in two of the subjects decidedly less work was done on the alcohol days, while in the other two there was no great difference. There was, however, a considerable increase from day to day as the result of practice, and as each alcohol day followed a normal day distinctly more work should have been done on the latter. The work of the first quarter of an hour was done on each day before the wine had been drunk, and it is therefore possible to show the special action on fatigue by expressing the results as percentages of that done in the first quarter of an hour.

Aschaffenburg has not used this method of demonstrating the effect of the alcohol, but when expressed in this way the figures show in each case a steady falling off during the last three-quarters of an hour (with an end-spurt in one case) on the normal days, while the chief characteristic of the alcohol days is their irregularity ; and it cannot be said, except, perhaps, in one case, that the decrease on the alcohol days becomes greater in the later periods of work.

When expressed in this way, the effect of the alcohol seems to have shown itself in a diminution of the capacity for work from the outset, and not to have had any special influence on the latter part of the period of work.

In spite of the very definite evidence of the effect of alcohol on the quantity of work, there did not seem to be any change in its quality, the proportion of errors being small and not different on the two sets of days.

Several researches have been recorded by Ach,[1] Maljarew-

[1] ' Psychologische Arbeiten,' 1901, Bd. iii., S. 203.

sky,[1] and Rüdin,[2] to show the effect of alcohol on the processes of perception and apprehension, but they do not in general give data to allow any estimation of the action of the drug on fatigue. Perhaps the most important result of Rüdin's work is to show how great may be the degree of insusceptibility to the action of alcohol in some persons. He used the large dose of 100 c.c. of absolute alcohol, and yet in some cases the effect was very slight in spite of the fact that the subjects of his tests were abstainers. This work shows that great variations in susceptibility to the action of alcohol may be present in those who have always abstained from the use of alcohol and need not depend on different degrees of habituation to its action.

I can now turn to a group of researches which derive their special interest from the fact that they deal with the problem, not of the immediate effect of alcohol, but with that of its influence when taken over a period of some length. We have seen that this problem has not yet been taken up in the case of muscular fatigue; but several researches devoted to the study of the cumulative effect on mental activity have been carried out by the Kraepelin school. These researches have dealt with the character of the work executed on a succession of days during which the subject was taking alcohol, as compared with a period during which no alcohol was taken. In a preliminary experiment Fürer[3] investigated the effect of a dose of 80 grammes of alcohol taken at night on the mental activity of the next day, as tested by the processes of addition, learning by heart, and association. He found a distinct decrease in the capacity for work, and this result was confirmed later by Rüdin,[4] at any rate, in some persons.

The first to investigate the effect of alcohol when taken

[1] See a paper by Kraepelin, 'Ueber die Merkfähigkeit,' *Monatschr. f. Psychiatrie u. Neurol.*, 1900, Bd. viii., S. 247.

[2] 'Psychologische Arbeiten,' 1904, Bd. iv., S. 495.

[3] See a paper by Kürz and Kraepelin, 'Psychologische Arbeiten,' 1901, Bd. iii., S. 450, and *Arch. f. Psychiatrie*, 1895, Bd. xxvii., S. 970.

[4] 'Psychologische Arbeiten,' 1904, Bd. iv., S. 1.

over a number of days was Smith,[1] who used the same mental operations as Fürer, and found a definitely injurious effect in two subjects, with doses varying from 40 to 80 grammes of alcohol. Only brief summaries of his work have been published, and the most fully reported work of this kind is that of Kürz and Kraepelin, who investigated several forms of mental activity, of which the most important from the point of view with which we are now concerned were addition and learning by heart. In one subject both kinds of work were carried out for half an hour on each of twenty-seven successive days. On six days no alcohol was taken; then for twelve days alcohol in the form of dilute spirits of wine, and in a dose equivalent to 80 grammes of absolute alcohol, was taken on each day, usually before going to bed; then for five days no alcohol was taken, and then again alcohol in the same manner for two days, followed by two normal days. The exact estimation of any effect is rendered very difficult by the presence of the increase from day to day throughout the experiment due to the effect of practice and by the fact that sufficient time was not allowed at the end for recovery from any effects which might have been produced.

The results with the addition method show, however, that after alcohol had been taken for about eight days there was a falling off in the amount of work, although an increase might have been expected, owing to the continuation of the effects of practice. The work remained below the level to be expected during the following five days of abstinence, but fell still further on the two succeeding days on which alcohol was again taken, to rise again when it was discontinued. Normal experiments on another subject made it probable that the whole of the latter part of the experiment, even on the normal days, was under the influence of the alcohol, and it is very unfortunate that the experiment could not have been continued for a sufficient time after discontinuing the alcohol to see if the subject of the alcohol test would have risen to a correspondingly high level of work.

[1] 'Psychologische Arbeiten,' 1904, Bd. iii., S. 451, and *Arch. f. Psychiatrie*, 1895, Bd. xxvii., S. 968.

The observations with learning by heart carried out by the same subject also showed an injurious influence, especially on the two alcohol days in the latter part of the experiment.

In a shorter experiment on another subject five normal days were followed by six alcohol days, and these by two normals; and here the chief feature was a very decided rise in the amount of work on the last two days, pointing to an injurious influence of the alcohol.

These experiments almost certainly show that the dose of 80 grammes of alcohol lowered the capacity for work, not only during the periods when it was being taken, but also for some time afterwards. It must be remembered that work was only done, however, for half an hour on each day, and the figures provide no data for the estimation of any special action which the alcohol may have had on the factor of fatigue.

Apart from the work of the Kraepelin school, the only research in which the influence of alcohol on the capacity for mental work has been tested is one by Partridge,[1] who investigated the influence of the drug on the rapidity of adding, reading, and writing, and found that a dose of about 30 grammes had little effect. There was, perhaps, an initial quickening, followed by some slowing, but the changes were very slight.

I have but little new work to bring before you relating to the influence of alcohol on mental activity, and even this bears little on any special influence that alcohol may have on fatigue, as distinguished from its general action on the capacity for work. The chief point of interest about it is that the effect of the alcohol was tested on the same person and on the same days as those on which muscular work was done. In the second of Mr. Webber's experiments with the ergograph the intervals were occupied with mental work in the form of multiplication, in which Kraepelin's *Rechenhefte* were used, the subject having to multiply four numbers

[1] *Amer. Journ. Psychology*, 1900, vol. xi., p. 374.

mentally, and write down the final figure of the product.[1] This work was carried on for twenty-five minutes in each interval of half an hour, time being thus allowed at the beginning and end for the subject to move from and back to the ergograph, and to make any necessary readings and adjustments of the instrument. In the fourth experiment with the ergograph the first and second intervals were occupied in the same manner with mental work—on some days with multiplication and on others with typewriting.

In each of these experiments the dose of alcohol or control was taken during the first set of ergograms, and, consequently, before any mental work had been done to act as a standard. It is therefore not possible to bring out any effect on fatigue by expressing the results as percentages of the work done before any dose has been taken, and I can only give the absolute amounts of work on the different days of each experiment—figures from which it is not possible to draw any positive conclusions owing to the complication introduced by the effects of practice and other causes of variation from day to day. I have not attempted to eliminate these effects by the employment of Kraepelin's methods of calculating coefficients of practice, not because I believe these methods to be wrong, but because the experiments with which I am concerned were not continued for a sufficient time to allow their satisfactory application.

The number of multiplications performed in each interval in the second experiment are given in Table I. In the first interval it will be seen that there is a definite increase from day to day throughout the experiment, and, except on April 10, when a dose of 5 c.c. was taken, the increase is fairly steady. The figures for the second interval, on the other hand, show a great increase on April 11, and the comparatively small increase on the following day, when 10 c.c. was taken, suggests an injurious effect of the alcohol; but the whole experiment was too short to allow any definite conclusion to be drawn. It will be remembered that in this experiment the effect of the alcohol was to increase the

[1] See Appendix V.

amount of muscular work, especially at the beginning, owing probably to interest and excitement; but the figures for the mental work show little trace of this stimulating action about twenty minutes after the dose had been taken.

TABLE I.

	April 8. Control.	April 9. 10 c.c.	April 10. 5 c.c.	April 11. Control.	April 12. 10 c.c.	April 13. 5 c.c.
1st interval ...	318[1] (6)	397 (5)	416 (3)	484 (2)	542 (2)	581 (7)
2nd interval ...	369 (5)	403 (3)	394 (3)	525 (3)	537 (8)	632 (4)

In the fourth ergographic experiment multiplication by the same method was done on nine days, on three of which a dose of 40 c.c. of alcohol was taken, on two a dose of 20 c.c., on two the control mixture, while on the remaining two no dose was taken. The total amounts executed in the twenty-five minutes of each interval are given in Table II., from which it will be seen that the increase due to practice is very much less than in the second experiment; in fact, if the first day be excluded, the effects of practice are so slight as to be almost negligible. Any effect of alcohol which might be present has thus a better chance of showing itself, but it is very doubtful whether any such effect is present.

TABLE II.

	May 18. No dose.	May 20. 20 c.c.	May 22. Control.	May 24. 40 c.c.	May 26. No dose.	May 28. 40 c.c.	May 30. 40 c.c.	June 1. 20 c.c.	June 7. Control.
1st interval	659[2]	753	673	698	751	701	736	771	792
2nd interval	707	735	740	755	766	774	785	780	762

Owing to the interval between the two last days of the experiment, little reliance can be placed on the figures of the last control day, for the effects of practice would have disappeared to a considerable extent during the intervening period. The figures for the remaining days are so irregular that no definite conclusion is justifiable; if the dose of 40 c.c. had any effect at all, it was slightly injurious.

The figures for the second interval are far more regular,

[1] It must be remembered that in each unit there were three processes of multiplication. The figures in brackets give the number of errors in each period.

[2] The figures give the number of multiplications performed in each period of twenty-five minutes during the intervals between the records of the ergographic work.

and here the increase due to the effects of practice, though very slight, is so steady from day to day that we may with some confidence exclude any definite alcohol-effect. If there is any effect at all, it is in favour of the larger dose of alcohol, and this comes out especially from the comparison of the amounts in the two intervals, for on each of the three days on which this dose was taken there is a decided increase in the amount of work in the second interval as compared with the first, while on several of the days on which nothing or the control mixture was taken the increase in the second interval is very slight, or even absent.

We can certainly say that any action of the alcohol was very slight, and perhaps the most definite indication of an effect is in the direction of increase during the second hour after the dose had been taken, and if so, it is noteworthy that this corresponds in point of time with the increase in the amount of muscular work in the same experiment.

In this experiment typewriting was done on the other days, on only one of which was the dose of 40 c.c. taken, while 20 c.c. were taken on two days, the control mixture on three days, and no dose at all on two days. The results for each interval are given in Table III., the quantity written being expressed in centimetres. It will be seen that though comparison of the beginning and end of the experiment makes it clear that there was some increase due to the effect of practice, the figures are very irregular, and little significance can be attached to them. There is certainly, however, no indication of any favourable action of the alcohol, and the one day on which 40 c.c. were taken shows a decided falling off in the second interval.

TABLE III.

	May 17. No dose.	May 19. Control.	May 21. 40 c.c.	May 23. 20 c.c.	May 25. No dose.	May 27. 20 cc.	May 29. Control.	May 31. Control.
1st interval :								
Quantity of work	832	824	841	884	883	847	871	902
Corrected errors	47	56	86	80	89	74	86	94
Uncorrected errors	26	30	38	26	39	27	21	31
2nd interval :								
Quantity of work	797	842	805	884	956	897	885	904
Corrected errors	86	71	80	92	140	99	107	127
Uncorrected errors	45	46	31	26	42	36	44	19

I have so far dealt only with the quantity of work done in each of the periods of twenty-five minutes in the intervals between the sets of ergograms. The quality of the work should give another means of estimating the influence of the alcohol on fatigue. The result of previous researches has been to show that the number of errors is generally so small with the method of addition that it furnishes little indication of the presence of fatigue.[1] The process of multiplication, as carried out in our experiments, is so much more arduous than Kraepelin's addition method that it seemed possible that the quality of the work might here be of value. The errors in the earlier multiplication experiment were therefore counted, and the number of each in each twenty-five minutes has been added in parentheses in Table I. It will be seen that the errors are so few in number that little importance can be attached to the small variations they show. The chief interest is that the small number of errors points to the process of multiplication having become very automatic. The subject noted during the experiment that, in spite of the complexity of the task as compared with the simple addition method, the whole process nevertheless seemed to become quite automatic, and could be carried on with little sense of mental effort, and the very small number of errors affords a definite indication that this introspective observation was correct.

The errors were also counted in the typewriting done in the intervals of the fourth ergographic experiment. Errors occur so easily in this operation that it seemed probable they would furnish some indication of an alcohol-effect if one were present.

The errors in typewriting fall into two classes—those which escape notice and those which are noticed and corrected—and the numbers of each are given in Table III. It will be seen that the latter are not very numerous, and so constant in number that they give not the slightest indication of an alcohol-effect. The uncorrected errors occur more fre-

[1] See especially Amberg, 'Psychologische Arbeiten,' 1896, Bd. i., S. 336, and Rivers and Kraepelin, *ibid.*, S. 656.

quently, and show an unmistakable tendency[1] to increase with the rapidity of the work, being most numerous in the second interval of the fifth day, when the amount of work reached its maximum. When this increase with rapidity of work is taken into account, there is no definite indication of any alcohol-effect.

These few experiments, designed to study the influence of alcohol on mental fatigue, give very inconclusive results; but I do not wish to lay any great stress on them, for I am far from being satisfied with the method according to which they were devised. I followed the customary method of Kraepelin, arranging that the work should be done after the drug had been taken, and trusted to the application of coefficients of practice to make the different days of an experiment comparable with one another. A study of the results has shown that the application of this method of correction would be very arbitrary and unsatisfactory, and I now believe that the only satisfactory procedure is that adopted in the ergographic observations of executing work on each day of the experiment before any drug has been taken, the amount of such work forming a norm with which to compare the work executed after the administration of the drug. In further work now in progress this is being done, and in the meantime all that can be said is that with the faulty method thus far employed there is no definite evidence that doses varying from 5 to 40 c.c. of pure alcohol have any decided effect in the one subject tested.

The only other research on the effect of alcohol that I have to record is one carried out in conjunction with Mr. McDougall, in which we used the latter's method of studying fatigue of attention, the general plan of the research being exactly the same as in the corresponding work on caffeine (see p. 45). The experiment lasted for nine days. Alcohol, in a dose of 15 c.c., was taken on three days, and one or other of two control mixtures on the remaining days.

[1] The same tendency has been found in arithmetical methods. See Rivers and Kraepelin, *op. cit.*, S. 658.

In Mr. McDougall's case there was no evidence of any alcohol-effect. In the first period of work there were 1,826 hits, while on one group of control days there were 1,822 hits, and on the other 1,883. In the second period of work the total number of hits on the alcohol days was 1,854, while on the two groups of control days the numbers were 1,740 and 1,824 respectively. In the latter case both sets of control days had a smaller performance than the alcohol days, but the difference between the alcohol days and one of the control days was very small. If the figures have any significance, they point to a slight stimulating effect of alcohol about three-quarters of an hour after it is taken.

In the experiment in which I was myself the subject there was more evidence of an effect. In the first period the total number of hits on the alcohol days was 1,523, while on the groups of control days the numbers were 1,582 and 1,769 respectively. In the second period the number on the alcohol days was still smaller, being only 1,414, as against 1,562 and 1,590 on the two groups of control days.

Any differences found on the different sets of days are certainly not due to the effects of practice, for the experiment was not begun till after much practice had been acquired, and the figures throughout the experiment show no evidence whatever of improvement during the nine days. If there were any improvement, it is wholly masked by the great variations from day to day.

In both cases there was nothing decisive in the form of the curves showing the number of hits in the successive rows; but, unfortunately, the dose was taken before beginning to work, and therefore we have no normal standard with which to compare the work of each day.

It must be pointed out that, though Mr. McDougall obtained only negative results in this experiment with a dose of 15 c.c. of pure alcohol, he found later[1] that 3 ounces of whisky produced a very decided increase in the number of failures to strike the dots; a smaller dose of 1 ounce also

[1] *Brit. Journ. Psychol.*, 1905, vol. i., p. 441.

diminishing the accuracy of aim, especially three-quarters of an hour after it was taken. These were, however, only single observations, and the earlier experiments show that the variations from day to day with this method are very great.

I may now sum up the general results which have so far been reached. In the case of muscular work, we have seen that there is definite evidence that small doses, varying from 5 to 20 c.c. of absolute alcohol, have no effect on the amount or nature of the work performed with the ergograph, either immediately or within several hours of their administration, the results previously obtained by other workers being almost certainly due to defects of experimental method. With a larger dose of 40 c.c., there was evidence—in one case, at least—of an increase in the amount of work under the influence of the substance; but the increase was uncertain and inconstant, and the possibility cannot be excluded that it was due to disturbing factors. With larger doses than 40 c.c., we have the work of Hellsten, showing a decided falling off in the amount of work with a dose of 80 grammes.

In the case of mental work, the available evidence points to a decrease in the amount of work under the influence of alcohol when there is an effect at all; but there are very great individual differences, even the large dose of 100 c.c. failing to show any effect in some persons.

All investigations on the action of alcohol on the capacity for muscular work, and most of that on its action on the capacity for mental work, have been directed to test the effect of the drug over the period immediately following its administration. As I have already pointed out, little has hitherto been done in the investigation of its prolonged action by comparing periods during which alcohol is taken with periods of abstinence. From the practical point of view, and especially from the point of view of the value of the habitual use of alcohol as an article of diet, this latter line of work is of far greater interest and importance than the former, but its experimental investigation is much more difficult.

The work which I have described in this and the last lecture has been so much devoted to the study of method, and the results have been so largely negative, that there is little need for theoretical consideration. The most salient fact which seems to require explanation is the combination of a stimulating action of alcohol on muscular work with a depressing action on mental work. It is true that these two effects have not yet been demonstrated on the same person and under the same conditions, and that even the separate actions cannot yet be said to be placed beyond all dispute ; but some observations may be cited which, while supporting the view that increased amounts of muscular work may be done under the influence of alcohol, at the same time help to explain its nature.

The different mode of action on muscular and mental activity suggests a double action of alcohol, such as I have supposed to exist in the case of caffeine, and the first point to be considered is whether we have any evidence of an action on the isolated neuro-muscular mechanism, such as is well established for caffeine. There is some evidence pointing to there being such an action, and, further, that this is of a stimulating kind.

Scheffer[1] has found that in the frog doses of alcohol amounting to one-thousandth of the body-weight produce a very great increase in the amount of work executed by the gastrocnemius of that side of the body to which the alcohol is allowed access, an action which continues for four hours, after which time there ensues a diminution in the amount of work as compared with the uninfluenced side of the body. As the result of experiments with curare, Scheffer came to the conclusion that the action was due to stimulation of the neural rather than of the muscular part of the neuro-muscular mechanism, and he suggests that this may be due to changes in the excitability of the nerve fibres of the kind suggested by the experiments of Waller.

A similar stimulating action of alcohol on the muscular

[1] *Arch. f. exp. Pathol. u. Pharmakol.*, 1900, Bd. xliv., S. 37.

activity of the frog has been found by Lee and Harrold.[1] Doses of 1 to 4 minims of a 10 per cent. alcohol per gramme of the frog increased the amount of work in some cases by more than 100 per cent.

The question whether this direct action which has been shown to exist in the frog will also account for the increase which has been found in man should be elucidated by the results of electrical stimulation with the ergograph ; but, unfortunately, the work on this point is not only very scanty, but contradictory, Lombard finding a decrease in the amount of work, while Frey records an increase, and in the face of this divergence we can only await the results of further inquiry.

In the only experiment in which I have found an increase in the amount of work under the influence of alcohol this increase occurred, not immediately after the administration of the drug, but at an interval of more than an hour, and it persisted for more than three hours after the alcohol had been taken. This late and prolonged action is very suggestive of the same kind of effect as that described by Scheffer, which, it may be noted, lasted for four hours, and it seems possible that a purely peripheral action, resembling that on the isolated muscle-nerve preparation, may, at any rate, have contributed to the increase.

It is probable, however, that this peripheral action is complicated by a central action, and assuming for the moment that alcohol—at any rate, in some persons and with certain doses—does produce an increased output of work, the nature of this central action may be briefly considered.

Kraepelin,[2] who believes that the effect of alcohol is entirely central, ascribes the increase in the output of work under its influence to the increased ease with which motor impulses are set up under the influence of alcohol. He apparently regards the increased work recorded in an ergographic curve as having the same cause as the increased talkativeness and tendency to act on impulse which is characteristic

[1] *Arch. ital. de Biol.*, 1901, t. xxxvi., p. 101.
[2] 'Psychologische Arbeiten,' 1901, Bd. iii., S. 636.

of alcoholic intoxication. The increased output of work would, according to this view, be due to the removal of some controlling influence, and we should expect in this case that the contractions of an ergogram under the stimulating influence of alcohol would be performed less regularly than in the normal condition.

The only worker who has noted irregularities in the contractions under the influence of alcohol is Hellsten,[1] but he notes their presence only after the administration of very large doses of alcohol—large enough to produce a distinct decrease in the amount of work. The observations on the general condition of the subject W., described in Appendix IV., show that in his case the regularity and delicacy of movement were affected, though there is no evidence that the ergograms themselves, or the contractions of which they are composed, were less regular than usual. It may be noted, however, that this general disturbance of movement was most pronounced in the prolonged experiment of July, 1906, when the alcohol did not produce any increase in the output of work.

That alcohol acts by removing some controlling influence is suggested by the effect of mental fatigue on the capacity for muscular effort. In the early work of Mosso with the ergograph it was found that in some persons mental fatigue could be associated with a decided increase in the output of work. In the case of one of his assistants, Professor Aducco, it was found[2] that the fatiguing, though at the same time exciting, task of giving an inaugural lecture increased the capacity for muscular work as tested by the ergograph, and I have found that I am an example of this mode of reaction in a condition of mental fatigue.

Repeated observations have shown that, when in a state of mental fatigue, I can execute ergograms distinctly above my average amount. In most, if not all, of the cases in which this increase has occurred, the mental fatigue has been induced by work which was decidedly interesting, and it is probable

[1] *Skand. Arch. f. Physiol.*, 1904, Bd. xvi., S. 184.
[2] Mosso, 'Fatigue,' London, 1904, p. 244.

that the increased capacity for muscular work found by Aducco and myself is usually due to the prolongation of the effect of this interest.

In at least one case, however, in which this kind of reaction occurred all trace of interest had so completely disappeared that it would seem very unlikely that the effect could have been due to this latter cause. At this time I was recording an ergogram every night before going to bed, and a good example of the average ergogram at this period of the day is that marked A in Fig. 13. The curve marked B was

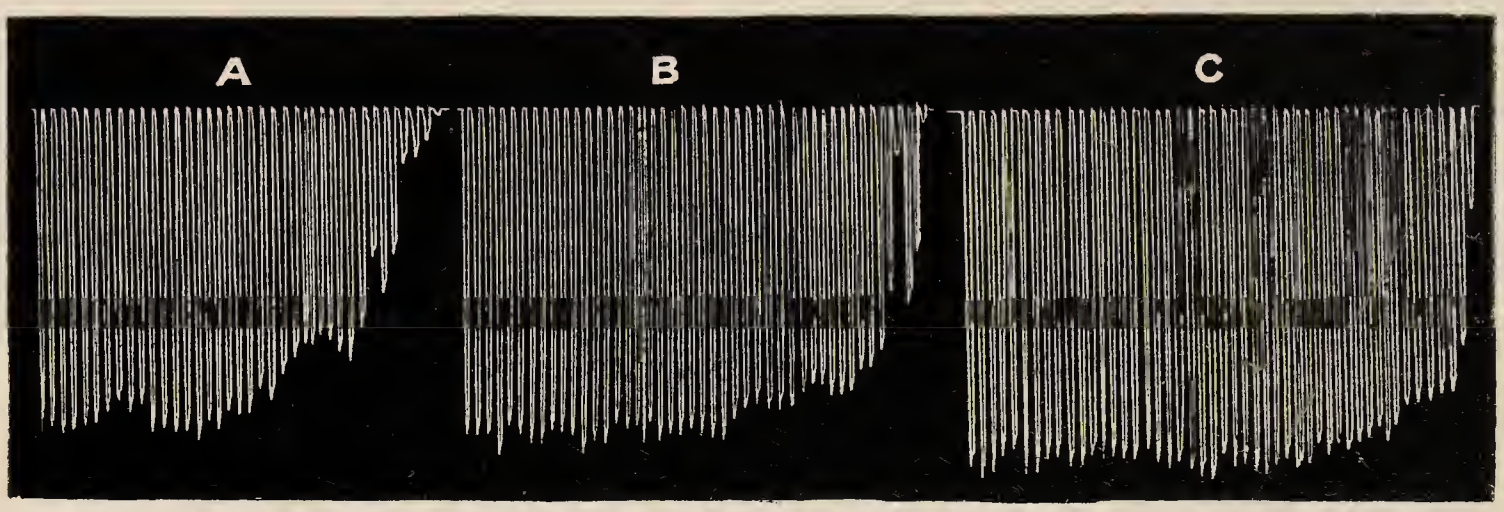

FIG. 13.

A, Normal; B, Mental fatigue; C, Alcohol.

	A.	B.	C.
Work (kilogrammetres)	4·8 (100)	6·7 (139)	8·3 (172)
Number of contractions	38 (100)	46 (121)	49 (129)
Average height (centimetres) ...	3·2 (100)	3·6 (113)	4·2 (131)

taken one night after a very fatiguing day, when I had read a paper in the evening and had reached my rooms at night so tired that it was only by a great effort that I brought myself to carry out my usual task of recording an ergogram. I seated myself, however, at the ergograph, and, to my great surprise, produced the curve B, very much larger than usual. I have added in the figure a third ergogram, C, taken after a dinner-party, at which I had had two glasses of champagne. This ergogram, the largest I have ever recorded, probably owes quite as much to the social intercourse and excitement of taking an ergogram under these circumstances as to any physiological action of the champagne, but this latter factor

was probably in operation to some extent. Thus we see that two very different conditions, enormously different subjectively, can produce very similar effects on the capacity for muscular work, as tested by the ergograph.

I bring forward this isolated, and it may be thought trivial, observation, because it seems to me that this similarity of action of alcohol and mental fatigue may give the clue to the explanation of the effect of the former.

The observation seems to show that a state of pronounced fatigue can have just the same effect on the capacity for muscular work as is produced by alcohol. In my condition of mental fatigue there can be no doubt that my capacity for the performance of mental work was lowered, and we have, therefore, in this observation an example of the same association of increased muscular activity with lower mental activity which there is reason to suspect is characteristic of the effect of alcohol. The observation strongly suggests that at least one action of alcohol may be to depress the activity of some higher nervous mechanism which serves to control and keep in check muscular activity, and that when this control is weakened, increased amounts of work can be executed.

I may, perhaps, consider for a moment the possible nature of this process of removal or weakening of a normal control. The idea which occurs most readily is that the weakening of control is due to the dulling of the sensations of fatigue, and that the action of alcohol is of this kind is rendered probable by the existence of the feeling of ease which has been recorded by many of those who have worked with the ergograph under the influence of alcohol. Such dulling might occur in two ways—it might be due to the direct influence of alcohol on the sensory centres, or it might be due to its indirect effect in promoting general excitement, during which the sensations aroused by the fatiguing work would remain below the threshold of consciousness.

There is another possible factor in the production of the stimulating effects of alcohol, which may be briefly considered. We have seen that emotional conditions have a very pro-

nounced influence on the ergographic curve, and it is almost certainly through its emotional aspect that interest acts. It is also probable that pleasurable emotions have a greater effect on the capacity for work than unpleasant emotions. It is an undoubted fact that alcohol in most people produces a pleasurable emotional condition, and it is the production of this condition which has been the chief motive in making the use of this substance so widely prevalent among mankind. It is possible that there is some kind of relation between the occurrence of pleasurable emotion and the increase of the capacity for muscular work. The exact mechanism by which the emotional condition acts is doubtful, but here again there is the possibility that it may be through dulling, absolutely or relatively, of the sensations of fatigue.

One provisional conclusion may be stated. We have seen that the condition of muscular activity may be affected in an apparently identical fashion by alcohol and by pronounced mental fatigue. This similarity of action should make one very chary in concluding that any stimulating effect of alcohol on muscular activity is an indication of a physiological action which is beneficial to the organism as a whole. But here I should like to say one word to those who are interested in the action of alcohol from the practical point of view. It is obvious that the problem of the nature of the action of alcohol on muscular activity is one of very great complexity, for the elucidation of which much more work is necessary ; and until this has been done, those interested either in the therapeutical or in the dietetical value of alcohol should hesitate before drawing any practical conclusions.

Before I leave the subject of alcohol, I must consider briefly a problem stated at the beginning of this lecture. Most of the previous work on alcohol has been done by using this drug in one of the forms in which it is employed in everyday life, and it is open to anyone to say that the stimulating effects of small doses which have been recorded by other workers are due, not, as I believe, to the neglect of the factors

of interest, etc., but to the action of other constituents of the alcoholic beverages which have been used.

We have already seen (p. 81) that in one subject a dose of whisky may produce an effect which is wholly absent with an equivalent dose of absolute alcohol, and though I believe that the difference was due to the presence of interest with the whisky, and its absence with the pure alcohol, this has not yet been demonstrated. A positive opinion on this point cannot be expressed till further experiments on this problem, now being carried out by Mr. Webber, have been concluded.

LECTURE IV (*continued*)

ACTION OF COCAINE, STRYCHNINE, TOBACCO, ETC.

Action of cocaine, strychnine, and tobacco; historical; new experiments with strychnine and tobacco—The work of Rossi and Féré—Action of formates, orchitic extract, 'fatigue antitoxin' and muscle extract—Conclusions; importance of control in method; results of new experiments and suggestions for future work—Analysis of fatigue-process—Individual differences.

I CAN now turn to the scanty record of work on the action of other drugs in fatigue.

COCAINE.

Of all the drugs which are supposed to influence the condition of fatigue, none has a greater reputation than cocaine. It is stated that the natives of South America are enabled to perform great feats of endurance under its influence, and to withstand severe hunger and thirst owing to its effect. This popular reputation is not belied by the results of experiment. The fullest work on the drug was published by Ugolino Mosso[1] in 1890, in which ergographic observations on himself formed only part of a systematic investigation into the physiological action of the drug. Experiments on dogs showed that in doses of 0·0005 gramme per kilogramme of body-weight of the animal no effect was produced on muscular activity; that 0·001 gramme per kilogramme had a stimulating effect; and that doses of 0·003 gramme per kilogramme diminished the amount of work performed by the muscle, or produced complete paralysis, the paralytic effect being very sudden when the dose was strong. Before this time Aschenbrandt[2] had found that

[1] *Archiv f. d. ges. Physiol.*, 1890, Bd. xlvii., S. 553.
[2] *Deutsche med. Wochenschr.*, 1883, S. 730.

doses of 0·1 gramme cocaine increased the resistance of soldiers to fatigue, and Freud[1] had shown that doses of 0·1 to 0·15 gramme increased the strength of contractions with the dynamometer. Mosso found that a dose of 0·1 gramme taken by the stomach had a decided effect on the amount of work produced by means of electrical stimulation of the muscle, the increase reaching 23 per cent. Further observations showed that the stimulating effect became more decided if the muscle were fatigued. After work had been done to exhaustion by means of electrical stimuli, a dose of 0·05 gramme had a very decided effect on the contractions produced by electrical stimulation, and a still more marked effect on voluntary contractions. Mosso also compared the effect of the drug in the fasting condition and after violent and prolonged exercise. In each state the drug had a most pronounced beneficial effect, both on the general condition, and on muscular activity as shown by the ergograph, the amount of work being doubled both with electrical and voluntary contractions. He concluded that the beneficial effect is—at any rate, in part—due to the direct action of the cocaine on the muscle, and that the drug is able to abolish the effects of fatigue directly, though he does not suggest any exact mechanism by which this can have been brought about. He combats the idea which had been previously suggested that the stimulating effect of cocaine is due to its action on the sensory side of the nervous mechanism involved, leading to a dulling of the sensations of fatigue ; but it must be noted that one of the most striking features of his own paper is the very graphic account of the disappearance of extremely severe sensations of fatigue under the influence of the drug. The next work, by Sobieranski,[2] on the action of cocaine I know only through an abstract, the original having been published in Russian. This paper is noteworthy for the fact that control injections were given to eliminate the effect of suggestion, which might be produced by the injections of cocaine. Sobieranski differed totally from Mosso in finding that the drug had no effect on

[1] *Wiener med. Wochenschr.*, 1885, S. 129.
[2] *Centralbl. f. Physiol.*, 1896, Bd. x., S. 126.

the work performed by means of electrical stimuli, while having a distinct effect on the work performed by voluntary contractions; and he concludes that the drug acts solely through the central nervous system. No indication is given in the abstract of the doses employed, and in the absence of knowledge about this and other experimental conditions, critical comparison is impossible. Another work on cocaine is that of Benedicenti,[1] who chewed the leaves of coca, and found that in consequence the amount of work with the ergograph was not only doubled, but that the effect lasted longer than that of other substances (tea, coffee, maté, and guarana) which had been tested under similar conditions.

It is probable that part of the increase which has been described as the effect of cocaine has been due to interest, etc., which Sobieranski alone attempted to exclude; but there can be no doubt that, in addition, there is a physiological effect on muscular activity, and it would seem that this stimulating action is most pronounced in the presence of fatigue, and especially of general fatigue. Its mode of action remains doubtful, and, in view of the conflict of evidence shown by the work of Mosso and Sobieranski, it must be left an open question how far its effect is due to a direct action on muscle, and how far to some action on the central nervous system. It will be noted that we met with a similar conflict of evidence in dealing with the effect of alcohol on the muscular contractions produced by electrical stimulation, and it is evident that this method of investigation is greatly in need of further study.

Strychnine.

The action of this drug has been tested with the ergograph by Rossi[2] and Féré. The former found decided increase in the amount of work, the effect being exclusively on the number of the contractions. His method was the same as that used

[1] Moleschott's 'Untersuch.,' 1899, Bd. xvi., S. 170.

[2] *Rivista sper. di Freniatria*, 1894, vol. xx., p. 464, and *Arch. ital. de Biol.*, 1895, t. xxiii., p. 56.

in his alcohol work. Ergograms were recorded for an hour, and he found no reaction at the end of this time.

Féré[1] tried the effect of a dose of 1 milligramme injected subcutaneously, and found a decided increase, followed by a fall below the normal, such as he finds with nearly all other drugs. When the strychnine was injected immediately before the ergographic record was taken, there was an initial decrease ; but this was due, doubtless, to the act of injection, and not to the effect of the drug.

Mr. P. C. V. Jones[2] has carried out an experiment with strychnine on the same general lines as the other work recorded in these lectures. Six sets, each of six ergograms, were recorded—the first two at intervals of half an hour, and the remainder with hourly intervals, so that the effect of the drug was followed for about five and a half hours. The whole experiment lasted for fifteen days, on four of which 7 minims of Liq. Strychninæ (4·2 milligrammes of hydrochloride of strychnine) were taken by the mouth, on four days the dose was 3 minims (1·8 milligrammes), and on the remaining days there was taken either a mixture containing gentian, which was quite indistinguishable in taste from the strychnine, or no dose at all. The experiment was complicated by the occurrence of a great diminution in the amount of work after it had been continued for some days, the diminution being especially great in the first ergograms of each day. This diminution did not take place gradually, but came on fairly rapidly after only three doses of strychnine had been taken, this making it necessary to consider separately the earlier and later portions of the experiment.

In each portion the drug produced an obvious effect. In the first, there was a rapid rise in the amount of work on the days on which the larger dose was taken, from which point there was a gradual fall ; but the curve did not pass below the normal till the fifth, to fall still further in the sixth. The curve for the smaller dose rose less rapidly, and

[1] 'Travail et Plaisir,' p. 297.
[2] *Journ. Physiol.*, 1908, vol. xxxvi., p. 435.

only fell below the normal during the last set. The form of the curve in each case was determined chiefly by the number of contractions.

In the second portion of the experiment there was a very great increase in the amount of work in the second set on the days on which the larger dose was taken, the amount being more than double that of the normal days; but here again the strychnine curve falls below the normal in the last two sets. The dose of 3 minims produced a smaller increase, followed by a fall below the normal, but here the difference was not very great. The action in the second portion of the experiment is more on the height than on the number of the contractions, this effect being doubtless associated with the diminution in the height of the early contractions, which seems to have been due to the cumulative action of the drug.

The effect of the strychnine is thus to produce a decided increase, followed by a reaction.

Tobacco.

The only other drug on which much work has been done from the point of view of fatigue is tobacco. The influence of this drug has only been tried when administered in the customary way by smoking, and I need hardly point out how in such a case the factors of interest and sensory stimulation must have full play. Both these factors always, so far as we know, produce an increase in the amount of work, and, therefore, it is significant that the evidence for the deleterious influence of this drug on the capacity for muscular work is perhaps more definite than in the case of any other.

The first worker with tobacco was Lombard,[1] who found that smoking had a very decided effect on the strength of voluntary muscular contractions. He found that one cigar of moderate strength could diminish the amount of work from 10·4 to only 2·1 kilogrammetres, the depressing effect passing

[1] *Journ. Physiol.*, 1892, vol. xiii., p. 44.

off soon after he ceased to smoke, though full power was not regained till more than an hour after the cigar had been laid aside. It is noteworthy that this result was wholly unexpected by Lombard, who had previously thought, as the result of general observation, that tobacco stimulated muscular activity. Lombard also tested the influence of smoking on the strength of the contractions produced by electrical stimulation, and found that tobacco in this case had no effect, so that he concluded that the depressing effect of the tobacco was on some part of the central mechanism.

The next research on the effect of tobacco is by Vaughan Harley.[1] This worker found that on himself the effect of tobacco was much less pronounced than had been stated by Lombard, but that on the whole its action was detrimental, though the effect was often within the variations which are found at different periods of the day. In 1901 the influence of tobacco was tested by Hough[2] on the work executed by means of the spring ergograph or dynamograph. He found no change in the constant fatigue level, but the fall to this constant level took place more slowly than on the normal days. This is the only experiment with drugs by this method which has been recorded, and we have no means of telling whether the opposite results of Hough and Lombard are due to the difference of method, or whether they depend on difference of individual susceptibility or other variation of the conditions of the experiment. The effect of smoking cigarettes has been investigated by Féré,[3] who found an initial increase, followed by a fall below the normal, when the subject began to smoke five minutes before the experiment began; but when the record was taken fifteen minutes after beginning to smoke, the action was purely depressing. In this case a second cigarette produced a very decided though transient increase after an interval.

I am able to give the result of brief experiments on two

[1] *Journ. Physiol.*, 1894, vol. xvi., p. 118.
[2] *Amer. Journ. Physiol.*, 1901, vol. v., p. 240.
[3] 'Travail et Plaisir,' p. 316.

subjects to test the effect of smoking a cigar after dinner. In one subject the work of two days with smoking was compared with that of three normal days, and in the second subject there were two days with smoking and two without. Ten ergograms were recorded at intervals of five minutes in one case and twelve in the other without any pause, and the smoking began after the first ergogram. Any kind of disguise was of course impossible.

The smoking was distinctly pleasant, and there was naturally strong sensory stimulation. All that we know of the effects of these two conditions would lead us to expect a very decided and immediate increase in the amount of work, altogether apart from any physiological effect, and it cannot, therefore, be regarded as without significance that any such increase was completely absent. There was no trace of any immediate increase, and on the whole a smaller amount of work was done on the days on which the cigars were smoked than on the intervening normal days. The decrease was not great, and probably not beyond the limits of normal variation, and the point I wish to emphasize is that there seemed to have been an inhibition of the effects normally produced by such a pleasurable and stimulating activity as that of smoking.

We thus see that tobacco comes out from the ergographic test less creditably than the other drugs we have been considering, though here, as in other cases, much more work is necessary before we can expect to understand the mode of its action. It is, however, noteworthy that the prohibition of this substance during training for feats involving muscular activity seems to show that this depressing action on the strength of muscular contractions has been recognized by general experience.

Other Drugs.

I have now considered the action of five drugs—caffeine, alcohol, cocaine, strychnine, and tobacco. Very little work has been done on any others, and most of this is due to two investigators, Rossi[1] and Féré.[2]

The Italian worker found that some of the substances he tested increased the amount of work, while others had a depressing effect. The former class, which he calls hyperkinetic, included caffeine, cocaine, alcohol, and strychnine, and also absinthe, camphor, and ether. The other class, called hypokinetic, included bromide of potassium, chloral hydrate, duboisine, hyoscyamine, opium, and morphine.

It will be noticed that this division into hyperkinetic and hypokinetic substances corresponds with the customary division into stimulants and sedatives. It would appear that there is a correlation between the action on muscular activity and the action on other vital processes. Among the hyperkinetic substances of Rossi, we have considered the action of three fully, and have seen that behind their apparent similarity of action there are very decided differences, and fuller investigation of the other drugs investigated by Rossi will probably render further subdivisions of his classes necessary.

The worker who has experimented most widely with drugs is Féré, but his work is unfortunately not of a kind to inspire much confidence. Nearly every drug is found to produce the same kind of effect—an initial increase followed by a fall below the normal, opium being, perhaps, the only substance among the many tested which differed greatly from the rest in showing a more pronounced depressing effect. Recently Féré[3] has published a paper, in which he shows that just the same kind of effect as that produced by taking these

[1] *Rivista sper. di Freniatria*, 1894, vol. xx., p. 442. A résumé is given in *Arch. ital. de Biol.*, 1895, t. xxiii., p. 49.

[2] Most of Féré's work has been brought together in his book, 'Travail et Plaisir,' Paris, 1904.

[1] *Revue de Médecine*, 1906, t. xxvi., p. 1.

drugs is also found after both tasting and swallowing 20 c.c. of a 20 per cent. solution of sugar; and Féré even believes that this substance is an accelerator of fatigue, as we have seen he supposes to be the case with caffeine and alcohol. It is very difficult to believe that the effects described by Féré can be due to the physiological effects of the substances he has used, and it is probable that in, at any rate, most cases his results give no indication of the true physiological action of the drugs he has used, but are entirely or predominantly due to the influence of interest on his muscular activity.

A few other researches on the action of drugs or other substances may be briefly mentioned. Clément[1] has found a decided increase in the amount of work with the ergograph after taking for three days formic acid neutralized with bicarbonate of soda; but there is no evidence that he did anything to eliminate the influence of interest.

The effect of orchitic extract on muscular activity has been tested with the ergograph by several workers,[2] most of whom have not employed any adequate control; but a very decided exception is to be found in the work of Pregl,[3] who gave the extract subcutaneously, and used control injections of glycerin and normal saline solution. Pregl desired to test, not the immediate effect of the extract, but its action over a prolonged period, and two subjects were used, one of whom was given the extract and the other the control injection, both being entirely ignorant of the aim and method of the experiment. It was found that the subject into whom the orchitic extract was injected executed a distinctly larger amount of work than in a previous normal period, while the subject who received only the glycerin did rather less. At the close of the series orchitic extract was injected for a period into the subject who had previously received the control injection, the extract producing a most decided effect on the amount of work.

[1] *La Semaine Méd.*, 1904, p. 100.
[2] See Zoth, *Arch. f. d. ges. Physiol.*, 1896, Bd. lxii., S. 335, etc.
[3] *Arch. f. d. ges. Physiol.*, 1896, Bd. lxii., S. 379.

Another research is one on the body isolated by Weichardt,[1] which he believes to be the antitoxin of fatigue. Weichardt only tested the effect of this substance on one person—a girl—and found an increase after its administration. He states that the influence of suggestion was excluded by giving the supposed antitoxin in a pastille, the nature of which was unknown both to the patient and her doctor, and he evidently believed that by this device he had excluded any possible disturbing factor of a psychical nature.

The last research to be mentioned is one by Slade[2] on the action of Liebig's extract of muscle, which was tested by the same general method as that used in other work recorded in these lectures, three sets of ergograms being recorded at half-hour intervals. A complete disguise was here impracticable, but interest and sensory stimulation were made as equal as possible by taking the extract on some days, white of egg in hot water on other days, and hot normal saline solution on others. The days on which the Liebig's extract was taken in doses of 15 grammes gave amounts of work which followed almost exactly the same course in relation to the initial ergogram as on the other days on which albumin or the saline solution were taken. The experiment gave a very striking demonstration of the closeness of correspondence which may be obtained between the curves representing the course of work of three groups of days when the general conditions are kept constant. The negative result of this experiment affords a valuable guarantee of the value of the ergographic method, and of the reality of the positive effects which have been obtained with more active substances.

Conclusions.

The chief interest of the work which has been recorded in these lectures lies in its bearing on method. It has been my chief object to illustrate the principles which should be followed

[1] *Münch. med. Wochenschr.*, 1904, Jg. li., S. 2125.
[2] *Journ. Physiol.*, 1907, vol. xxxv., p. 163.

in the study of pharmacology when the subject is the living man. One point of method has, I hope, been clearly established—viz., the absolute necessity that experiments with drugs on man should be carried out with adequate control, designed to exclude the influence of interest, sensory stimulation, and suggestion. Further, I have been able to show that this control is possible even in the case which seemed to me at first most hopeless—that of the administration of alcohol by the mouth. It is possible so completely to disguise the characteristic flavour that the subject of the experiment may be quite unaware whether he is taking alcohol or some inactive substance.

Although I wish to lay stress chiefly on the importance of my results in connexion with method, I do not wish to neglect the actual contributions to the knowledge of the action of drugs, which are provided by the experiments I have described in these lectures. In the case of alcohol the chief result has been negative, having shown that the effects previously recorded as those of small doses of alcohol are not true physiological effects, but merely the consequences of faulty methods of investigation. With larger doses of this substance no conclusive results have so far been reached, but enough has been done to point the way for further work, which is now being carried on by Mr. Webber.

The chief result of the work with caffeine is the strong suggestion it affords that this drug has a double action on the mechanism concerned in muscular work, while the work of Mr. Jones with strychnine provides a very striking demonstration of the stimulating action of a drug.

The negative results with small doses of alcohol and the inconstant results with larger doses might possibly be held to suggest that the ergographic method is ill suited for the study of the action of drugs on fatigue, and the great value of the experiment with strychnine and of my own final experiment with caffeine is that they enable us to reject such a suggestion decisively. These results show that the ergographic method is capable of bringing out drug-effects in

the most decided manner, and a study of all the work recorded in these lectures can leave little doubt that the negative effect with small doses of alcohol is due to the absence or to the very small amount of any influence on the process of muscular fatigue.

I should like here to repeat and emphasize the statement that the work described in the lectures has dealt almost entirely with one department of the subject—viz., the investigation of the immediate action of drugs on the physiological mechanism taken as a whole. I have hardly touched on the question of the effects of these drugs when taken over prolonged periods, nor have I dealt at any length with the methods by which we may hope to effect an analysis of the general action into the constituent actions on different parts of the organism. I have brought forward evidence in favour of complexity of action in the cases of both alcohol and caffeine, but have not attempted to apply these methods of analysis—viz., the investigation of the action of the drugs on the fatigue induced by electrical stimulation of nerves in man, and the study of the action of drugs on animals or on the different parts of the isolated neuro-muscular mechanism.

One interest of the use of drugs from this point of view arises out of the expectation that it may throw light on the analysis of the fatigue-process itself. It was from interest in this latter problem that I first undertook experiments with drugs. It seemed to me that in the use of drugs lay the chief hope for the discovery of the seat of muscular fatigue. If we could find a drug which could be shown to be without action on the isolated peripheral mechanism, but which influenced the ergogram recorded by the living man, we should have a definite instrument for the detection of the part taken in the formation of the ergogram by central factors. On beginning work I soon obtained evidence of the unsatisfactory nature of previous researches on the capacity for muscular work in man, and I have so far been occupied in repeating these researches with methods designed to exclude

what I believe to be disturbing factors. The result has made it clear that neither in alcohol nor in caffeine have we a drug with a simple action, and they are, therefore, ill suited for the purpose of the proposed analysis.

Such a substance is probably to be found in strychnine, but at present we have too little work with this substance to enable us to define its mode of action on the work executed with the ergograph, the experiment described in this lecture showing an action on the number of contractions at one time and on the height at another.

It is in this differential action on number and height of the muscular contractions that the means of analysis have so far been sought. Kraepelin believes that action on the nervous system shows itself predominantly by an effect on the number, while action on the muscular system affects chiefly the height of the contractions. Some of the facts recorded in these lectures seem to be in agreement with this view. In my last caffeine experiment there can be little doubt that the effect was due to the central action of the drug, and in this experiment the increase was almost entirely on the number of contractions; and in the earlier and less complicated part of Mr. Jones's experiment with strychnine, which almost certainly has a purely central action, it was also the number of contractions which was increased.

It would be very dangerous, however, to conclude that because in some cases a drug, acting through the nervous system, increases the number of contractions, therefore such an effect on number demonstrates a central action. It is very doubtful whether the kind of evidence brought forward in these lectures can ever furnish satisfactory data for the analysis of the physiological processes concerned in muscular fatigue, which must rather be sought in the comparison of the work performed volitionally with that executed when the muscles are made to contract by electrical stimuli applied to the peripheral nervous mechanism, when any effect on central activity can be excluded with certainty. But few observations of this kind have hitherto been made, and those few are very

unsatisfactory, the whole technique of this mode of attacking the problem requiring to be reconsidered.[1]

In conclusion, I should like to refer to one aspect of the subject, an aspect which is of especial interest to myself. The branch of psychology in which I am chiefly engaged is that to which the name of individual psychology is usually given. It is that branch of psychology which deals with the differences in the mental constitution of different people, and by an extension of the term to the differences which characterize the members of different races. The physician is interested in this subject, owing to its bearing on those differences of temperament or constitution which influence the incidence of disease and the reaction to therapeutical measures, and I had this point among others in my mind when I stated at the beginning of these lectures that I hoped to show how the science of experimental psychology might be of service to medicine. Of the various means by which we may study these individual differences none is more hopeful than that which may be called the pharmacological method.

It is a matter of general experience that different persons are susceptible in very different degrees to the influence of drugs. The material I have brought forward in these lectures will have been sufficient to show how careful we should be in ascribing such differences to definite variations of physiological constitution. There can be little doubt that many of the differences which have been found by previous workers are due to variations in the part played by the psychical factors which have been allowed to complicate most work on this subject. In the experiments recorded in these lectures, however, these disturbing factors have been excluded, and yet there have been found—at any rate, in the case of caffeine—very striking divergencies in action in the two persons tested, and there can be little doubt that these are due to a definite difference in the incidence of the action of the drug. These

[1] In the older observations with the earlier forms of Mosso's ergograph it is very improbable that the same muscles were in action throughout the two kinds of experiment.

experiments leave little doubt that variations in the action of drugs on different persons may have their basis in deeply-seated physiological variations, and I believe that the study of these variations of susceptibility may do more than perhaps any other line of work to enable us to understand the nature of temperament and the relation between the mental and physical characters which form its two aspects.

APPENDIX I

FORM OF THE CURVE REPRESENTING THE COURSE OF FATIGUE

It is usually supposed that the course taken by the process of fatigue may be represented by a curve which remains approximately level for a time and then falls more or less rapidly, corresponding to a diminution in the amount of work, this idea as to the form of the curve being probably based on the nature of the ergogram of Mosso, which has usually been supposed to represent the course of the normal process of fatigue.

It has been seen (p. 4) that three different methods of studying the process of muscular fatigue agree in showing a diminution of capacity coming on soon after beginning to work, so that the curve falls, at first rapidly and then more slowly, till it passes into a horizontal line representing a condition in which the amount of work which can be performed remains constant for a considerable time. Such a curve, with its concavity upwards instead of downwards, which is obtained with the dynamograph, agrees in its general features with that found by Treves by means of his ergograph with variable weight; and, as I have pointed out, the ergograph with constant weight gives the same result if attention be paid to the course of the work of a series of ergograms and not to that of a single ergogram. To show to how constant a level a series of ergograms may attain, I give figures for two sets of observations in which ergograms were performed at intervals of two minutes without the breaks which I have usually adopted to demonstrate the action of drugs. In an experiment in which Mr. Webber recorded ergograms at intervals of two minutes for about three hours, the figures for the average ergograms of three normal days expressed in kilogram-metres ran as follows: 3·4, 2·9, 2·7, 2·3, 2·3, 2·2, 2·2, 2·1, 1·8, 2·0, 2·0, 2·0, 1·7, 1·6, 1·6, 1·8, 1·5, 1·9, 2·0, 2·1, 2·0, 1·9, 2·0, 2·0, and so on. In a similar series by myself the work of the ergograms ran as follows: 3·3, 4·1, 4·6, 5·0, 5·3, 3·2, 4·5, 3·2, 4·3, 3·4, 4·0, 3·2, 3·1, 3·1, 3·1, 3·1, 3·2, 3·2, 3·0, 3·0, 3·0, 3·0, 3·1, 3·1. This series thus showed at first the irregularities which characterize my work with the ergograph, but finally settled down to a constant level.

Three different methods thus agreeing in the demonstration of the course of normal muscular fatigue, the question arises whether mental fatigue does not follow the same course, and there is much reason to believe that it does. One of the most constant features of the curve of work obtained by any of the Kraepelin methods is a fall in the second five minutes, often continuing into the third period of five minutes. This fall has usually been ascribed to the effect of spurt, which undoubtedly contributes to the formation of this early portion of the curve of work. Recent research has shown that, when work by Kraepelin's methods is carried out for short periods of ten minutes,[1] there is evidence of a diminution of capacity which would seem to be due to fatigue ; and, if so, part at least of the early fall of the curve must be due to the presence of this factor, the rise of the curve, due to practice, only showing itself after the fatigue process has reached what would, in the absence of practice, have been its constant level.

The new method of McDougall would seem to afford a means of putting this to the test. Introspection, when using this method, gives one the impression that there is an early diminution in the power of keeping up the attention to the high level demanded by this method, and it would seem that this early fall is followed by a period in which there is a more or less constant level of accomplishment. We have not yet sufficient data to enable us to tell whether the objective record corresponds with the subjective experience, but experiments now in progress with new apparatus (see Appendix II.) may be expected to show the nature of the curve representing the course of mental fatigue.

[1] Specht, *Arch. f. d. ges. Psychologie*, 1904, Bd. iii., S. 245 ; and Wimms, *Brit. Journ. Psychol.*, 1907, vol. ii., p. 153 ; Hylan and Kraepelin, 'Psychologische Arbeiten,' 1904, Bd. iv., S. 454.

APPENDIX II

NEW APPARATUS FOR THE APPLICATION OF MCDOUGALL'S METHOD OF STUDYING MENTAL FATIGUE

The apparatus used by Mr. McDougall[1] consisted of a large rotating cylinder, round which was placed a sheet of paper covered with eight rows of dots, which, when the cylinder rotated, passed in rapid succession behind an aperture in a screen placed before the cylinder. This method only allowed work to be continued for a limited time, amounting in the experiments recorded in these lectures to about three minutes. Further, the act of moving from one row to the next formed a disturbing factor, which might either distract the worker or act as an incentive to spurt. The chief feature of the new apparatus[2] is the use of a continuous Morse tape on which dots are printed as on Mr. McDougall's sheets. This tape passes over rollers put into motion by clockwork driven by a falling weight, and the time during which continuous work can be done is only limited by the distance through which the weight can fall. In my machine this time is ten minutes, but with the short intervals necessary for winding up the weight, work could, of course, be continued for a period of any length. The rate at which the dots pass behind a slit placed in front of the tape can be varied within wide limits by means of an arrangement which need not here be described in detail.

One advantage which this machine possesses over all other means for measuring the amount and nature of mental work is that the indication of the amount of work done in successive intervals of time involves no activity on the part of the subject of the test, but can be measured afterwards in terms of length of tape, provided that the rate of movement of the tape is constant. In all the ordinary methods of studying fatigue, the subject has himself to mark off the limits of the intervals of time into which the whole period of work is divided. One result of this in some subjects—certainly it is so in myself—is that there is a spurt at

[1] *Brit. Journ. Psychol.*, 1905, vol. i., p. 435.

[2] This apparatus has been made by the Cambridge Scientific Instrument Company.

the beginning of each interval, and this makes it impossible to study the natural time relations of the spurts, which, as introspection shows, occur not only at the beginning and end of the total period of work, but throughout its whole course. The new method allows an exact study of the variations of volition upon which the spurts depend.

Owing to much delay in the completion of the instrument and of the machinery for printing the dots on the tape, little work has so far been carried out with the machine, but enough has been done to show without doubt that by means of it very decided effects can be produced which are undoubtedly due to mental fatigue. As I have stated in the first lecture, there is some doubt how far the methods used by the Kraepelin school really measure fatigue, and certainly, as means of showing the influence of mental fatigue on various kinds of activity, they are singularly ineffective. With this new method, on the other hand, there can be not the slightest doubt as to the reality of the fatigue which is induced, and ten minutes' work with this instrument is capable of producing an effect on the capacity for muscular work, as shown by the ergograph, which far exceeds anything produced by the ordinary methods of inducing mental fatigue experimentally.

APPENDIX III

GENERAL ACTION OF CAFFEINE

The experiments to test the influence of caffeine on muscular activity, described in the second lecture, showed a very striking difference between the two persons who were the subjects of the tests, and I propose to give here some further observations which show equally decided differences in the general action of the drug. Throughout the whole of the experiments notes were taken of any conditions which might influence the results, including observations of an introspective nature, and in his work with the ergograph Mr. Webber noticed nothing which he could ascribe to the general action of the drug, this absence of general effect being associated, as we have seen, with only a slight action on muscular activity. In my own case, on the other hand, there were in some experiments such definite general effects as to leave no doubt that they were due to the action of the drug.

It is often difficult to distinguish between the direct physiological effects of a drug and those due to the knowledge that it has been administered, and the special point of importance in the observations I am about to describe is that they were made in the absence of knowledge which was rendered possible by the use of a control. In my first experiment to test the influence of caffeine on typewriting I seemed to be generally stimulated on the caffeine days; but as no control was used in this experiment, the feeling of stimulation might have been due to knowledge and consequent interest. In my second typewriting experiment I did not experience this sense of general stimulation during the actual observations, but noticed that I walked more vigorously, especially uphill, after the morning work on certain days, these days being found afterwards to have been those on which caffeine had been taken. The most decided effect, however, was on the amount and nature of the sleep at night. During the first half of the experiment I took on certain days a dose of 0·3 gramme of caffeine at about 5.30 p.m., the same dose having been taken in the morning. It soon became so obvious that my sleep was being affected that I discontinued the evening dose of the drug during the second half of the experiment. The effect of the caffeine

was to make me sleep very lightly, with many dreams and frequent waking, my sleep being as a rule sound and dreamless.

In my earlier experiments with the ergograph, in which a dose of 0·3 gramme was taken in the middle of the day, no general effects were noticed, with the exception of some sense of stimulation, and no effect on the capacity for sleep was detected. In my last experiment with caffeine, in which the dose was 0·5 gramme, the general effects of the caffeine were, however, very decided, and to illustrate their nature I give a brief abstract of my notes.

On the evenings from August 30 to September 3, the final day of an alcohol experiment and normal days, I was very sleepy in the evenings and slept soundly at night. September 3 was the first day of the caffeine experiment, and I was wholly unable to detect the nature of the dose, which was from the control mixture. On September 4 the dose was of caffeine, but I was not able to recognize that it was in any way different from that of the day before. Two hours later I noted a feeling of malaise,[1] which became very pronounced half an hour later, but had disappeared three and a half hours after taking the dose, to be replaced by a slight headache. I did not seem to be especially stimulated at the time or afterwards. That evening I was neither tired nor sleepy; I slept much less soundly than previously, and did not feel so refreshed in the morning. On September 5, the dose being from the control mixture, I noted that there was no malaise, as on the preceding afternoon, and that evening I was very tired and sleepy, and slept soundly.

On September 6 the dose was of caffeine, and half an hour after taking it I experienced a sense of stimulation. This was still present three-quarters of an hour later, though at the same time there was a feeling of malaise like that of two days earlier; at the end of the experiment there was a slight headache, though I still seemed to be stimulated. The following day was a control day: no note was made of any abnormal sensations, and after a very sleepy evening I had a thoroughly good night.

On September 8, twenty minutes after taking the dose, again of caffeine, I noted great mental activity, ideas about the experiments following one another in rapid succession—a state of mind which was very pleasurable, though recognized to be quite out of place in the middle of an experiment. The accompanying ergograms were larger than normal, though not to any very great extent. At the end of this set, half an hour after taking the dose, I was feeling very energetic, and this feeling continued, although accompanied by a definite headache. That

[1] This feeling was probably of the kind which is so often described by patients as one of 'sinking.'

evening I was not at all sleepy, and I had a wakeful night, with the sleep much disturbed by dreams. It seemed so unsatisfactory to make the following day part of the experiment that I did a day's work of the usual kind, but without any dose, and slept very well at night. After the work of the following day—a control day—I slept fairly, but I was so out of sorts on the next morning that I decided to stop the experiment.

It is of course possible that my disturbed sleep had no connexion with the caffeine, and I have given the record in some detail in order that my readers may form an estimate for themselves as to the relation between the administration of the caffeine and the sleeplessness. Of one thing I can be certain—viz., that the effect was not due to knowledge of the fact that I had taken caffeine. It was, of course, natural that the sense of stimulation on the caffeine days should have made me suspect that I had taken caffeine, but it never occurred to me for a moment that a dose of caffeine taken in the middle of the day would influence my sleep nine or ten hours later, and I need hardly say that the arrangement of the experiment would have been very different if I had suspected such a possibility.

There can be no doubt that this influence of caffeine on the capacity for sleep was due to a central action, and we may regard these general effects as additional evidence that the great increase of muscular activity shown by the ergograph had also a central seat.

My work with caffeine also illustrated the effect of giving up the habitual use of this substance, and the pronounced nature of these effects affords additional evidence that I am unusually susceptible to the influence of caffeine. When planning my first research with this substance, I gave up the use of tea and coffee about a week before the beginning of the experiment. This was followed by a condition of lowered physical and mental energy, which seemed to me to have much the same general character as that which is known to follow breaking the habit of taking more powerful drugs, and the neurasthenic condition produced was probably one of the reasons for the unsatisfactory nature of the experiment which followed. The experiment was carried out during a period of very hot weather, and I was inclined at the time to put down my condition of lowered energy to this cause. At the end of the experiment I again began to take tea and coffee, but on giving up their use a second time before a projected experiment a similar neurasthenic condition recurred. It seemed probable that this was due to the sudden breaking of what must probably be called a drug habit, and I therefore decided not to undertake a second experiment till the use of tea and coffee had been given up for a time long enough to

make it certain that the breaking of the habit could have no possible influence on the general state of health, and during the following two years, while experiments were in progress, I abstained completely from the use of tea, coffee, and cocoa.

I do not regard it as certain that these phenomena, which followed the act of giving up the use of substances containing caffeine, were its direct consequence. The association was only observed twice, and the abnormal condition in each case may possibly have had some other cause. My object is only to draw attention to the possibility that the cessation of the use of even such familiar substances as tea and coffee may have results the same in kind, if not in amount, as those following the cessation of the use of more potent drugs.

APPENDIX IV

GENERAL EFFECTS OF ALCOHOL

Contrary to what was found in the case of caffeine, the general effects of alcohol were decidedly more pronounced in Mr. Webber than in myself. This was probably due to the fact that the former had always been an abstainer, so that, not only were the effects of the drug probably more pronounced, but, as they were also quite new to him, they attracted more attention.

Even with the dose of 40 c.c. I noticed very little to differentiate the alcohol days from those on which only the control was taken. There was on some days, within an hour after taking the dose, a feeling of fullness in the head, which I know to be one of the results of taking wine, but this was not sufficiently constant or pronounced to enable me to recognize with certainty the days on which alcohol had been administered.

In Mr. Webber's case, on the other hand, the introspective observations were much more definite. Very soon after taking the dose of 40 c.c. of alcohol, it was often noted that there was some salivation, sweating, and irritation of the skin. Of these, the salivation was the most definite and constant. There was often salivation on the control days, but it was more obvious and lasted longer on the alcohol days.

As regards the sweating, it must be remembered that the prolonged experiment with the larger dose (see p. 85) was carried out in very hot weather, when a dose of any kind increased the natural tendency to sweat; but the sweating was noticed to be greater on the days which turned out afterwards to have been those on which the larger dose of alcohol had been taken.

Several times tingling of the skin, especially of the scalp, was noted, often accompanied by flushing. These symptoms occurred immediately after taking the dose, and were soon followed by a sensation of giddiness, which lasted for some time, often for as long as three hours.

Not long after taking the alcohol, probably within half an hour, there came on certain other symptoms, of which the most obvious subjectively were lassitude and disinclination to use either mind or body.

Every care was taken by the subject, however, to keep the experiment running smoothly, for it was known that, if anything went wrong, there would arise the necessity for action which the subject was anxious to avoid.

It was almost certain that the movements were slower than usual. In the normal condition the two minutes between successive ergograms were ample for the customary readings and adjustments of the ergograph, but on the 40 c.c. days the period of two minutes was hardly long enough to do what was necessary, although the time seemed no longer than usual. This was so striking that the subject was at first inclined to believe that the watch was in error, for it seemed to him that he had been carrying out his usual task at the normal speed.

The control of movement did not seem to be as good as normal. Several small accidents happened on days on which the dose of alcohol was 40 c.c., and these were probably the result of awkwardness in adjusting the apparatus. Some of the intervals were occupied in drawing lines for tabular purposes or in pasting ergograms in a book, and these operations were found afterwards to have been done roughly or irregularly on the days on which the larger dose of alcohol had been taken.

During the state of lassitude there was decided irritability; and a fellow-worker during the long experiment of July, 1906, states that he was able to recognize clearly the days on which the larger dose had been taken by the general demeanour of the subject—partly by means of the lassitude, partly by the very obvious irritability.

It is doubtful how far the state of lassitude was preceded by one of exhilaration, but, if it occurred, it was certainly of very brief duration.

It is especially noted that these effects of alcohol at first tended to arouse interest, but after a day or two this ceased, and the only desire of the subject was to carry out the appointed work of the day without disturbance, with no feeling of interest in its result.

These pronounced general symptoms only occurred on the days on which the dose of alcohol was 40 c.c., and they were much more noticeable in the second experiment with this dose. With the dose of 20 c.c. giddiness was occasionally noticed, and the other early symptoms may possibly have been present to some degree, but they were not sufficient to enable these days to be distinguished. With the smaller doses used in the earlier experiments any general effects of the kind just described were completely absent.

APPENDIX V

THE MULTIPLICATION METHOD

In order to make mental work more arduous than that usually employed to induce fatigue, a method was employed to test the action of alcohol in which the operation of adding two numbers was replaced by the multiplication of four numbers, a method which has also been adopted and described by Mr. Wimms.[1]

In order to make Kraepelin's *Rechenhefte* suitable for this modified arithmetical method, it was found necessary to make several changes. The rows of figures in these books consist of all numbers from 1 to 9, and the first step was to get rid of the figures 1 and 5, replacing them by other numbers. The necessity of doing without the figure 1 in a multiplication method is obvious; and even if 5 had not been an especially easy figure to multiply, it would have been necessary to get rid of it, owing to its becoming 0 when multiplied by an even number. After working for a time, it was found that 6 was also an unsatisfactory number. It was noticed that any even number multiplied by it remained the same, and this rendered multiplication by this figure so simple an operation in many cases that it was not comparable with others.

At first the figures to replace 1, 5, and 6 were chosen on account of similarity of form to those erased, 1 being changed to 7 or 4, and 8 or 3 being substituted for 5. Later, care has been taken to make such substitutions as will avoid products ending in 1, and a preference has also been given to odd numbers, owing to the great preponderance of even products which result if even and odd numbers occur with equal frequency.

[1] *Brit. Journ. Psychol.*, 1907, vol. ii., p. 153.

INDEX

THE END

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